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BRITISH JOURNAL OF SOCIAL MEDICINE

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LONDON
BRITISH MEDICAL ASSOCIATION
TAVISTOCK SQUARE, W.C.1

YEARLY SUBSCRIPTION (4 NUMBERS) 25s. U.S.A. $6.00 SINGLE NUMBER 7s. 6d.

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Brit. J. soc. Med. (1948), **2**, 123-131.

SICKNESS AND STRESS IN OPERATIONAL FLYING

BY

D. D. REID

Lecturer in Medical Statistics, London School of Hygiene and Tropical Medicine, University of London
Formerly Squadron Leader, Directorate-General of Medical Services, Royal Air Force

To the medical branch of an air force, the social or environmental conditions of pressing importance are the psychological stresses inevitable in air warfare. Only in war is it possible to observe the effects of such factors as acute hazard and intensive operational effort, with their resultant anxiety and fatigue, on the performance and well-being of such a highly selected population as the air crews of the Royal Air Force. Both the immediate effects of these stresses on efficiency and the long-term results in health were, therefore, the urgent concern of those whose duty it was to minimize these effects by every means open to the medical branch of a combatant force. The central issue was one of limitation of spells of duty—either short term, where the effects of hours of prolonged attention were to be forestalled, or long term, where the limits of an operational tour had to be set at a level high enough to ensure an adequate operational return for the training investment made yet not so long as to endanger health and morale. The problems of peacetime practice in social and industrial medicine are hardly as dramatic, yet the essential mechanism of the adjustment of men to the less hazardous but frequently harassing conditions of post-war life are identical. This account of some typical studies of sickness in relation to measurable environmental and personal factors is given in the hope of displaying the potentialities of the methods used in the study of problems of sickness and morale in an industrial population.

Research on duty limitation in the R.A.F. during the war had a tripartite approach by clinical, laboratory, and field surveys. The clinical studies have been described by Symonds (1943), the laboratory work by Russell Davis (1948); in the present paper is set out an application of statistical methods to data collected in the course of active operations in the field.

Background of Present Study

The background to the present studies may be briefly sketched. In the world war 1914-18, work was mainly along clinical lines, the opinions expressed (Birley, 1920) being intuitive judgments based on extensive experience with cases of neurosis occurring in the operational squadrons. The importance of the hazardous, fatiguing, and often physically exhausting nature of flying duties was recognized, but the issue was clouded by a preoccupation with the cumulative effects on health and performance of the physical stresses specific to flight, such as oxygen lack, and others less specific such as cold, noise, discomfort, and glare. A tendency to overstress the importance of the presumed cumulative effects of the stresses of air fighting as a cause of breakdown in flying men persisted until the world war 1939-45, and with it the implication that a simple relation existed between the number of hours' flying done and the resultant degree of deterioration in health and efficiency. Thus in the short term context, efficiency would fall off towards the end of an operational sortie, while in the long run, signs and symptoms of impending breakdown were to be looked for after a prolonged tour of many sorties.

Contrary indications, however, came from laboratory experiments recently described by Russell Davis (1948) where, in a complex and distracting experimental situation analogous to flying, no progressive deterioration in efficiency was observed. On the other hand it became clear that anxiety and tension had much more serious effects on the level of performance. This was strikingly confirmed by an analysis of the errors made by navigators of bomber aircraft during sorties against German targets (Reid, 1947). The effect of anticipatory anxiety was seen in a steady deterioration in efficiency on the outward journey, particularly over the enemy coast, and on approaching the target. This effect reached a maximum in the acute anxiety engendered by heavy enemy fighter opposition and persisted as long as the aircraft was over enemy territory. Compared with this, any effect of "fatigue," in its conventional sense of deterioration at the end of prolonged activity, was minimal. Similarly, Bradford Hill and G. O. Williams (1943) showed that landing accidents were no more common after long sorties than after much shorter ones.

Clinical studies by Symonds and D. J. Williams

(1947) on the histories of cases of neurosis arising in the operational Commands demonstrated that the bulk of them were men of neurotic predisposition who broke down early in their operational career. There did remain, however, many instances of breakdown after prolonged stress among men of the toughest fibre. Tour limitation, therefore, was essential, and in the formulation of policy in this matter the precision of statistical methods complemented the insight of the clinical approach. A search for objective measures of the process of adaptation to stress during the course of an operational tour showed that the critical nature of the early part of the tour was revealed by a simultaneous increase in the incidence of psychological disorder and the frequency of reporting sick and a fall in the average weight of a large group of flying men (Reid, 1947). As adjustment to the strain took place, these three indicators tended to stabilize at a new level and showed no sign of deterioration towards the end of a tour limited to thirty bomber sorties. The possibility of using such measures in the determination of optimum tour limits was thus evident, but there remained the task of discerning the relative importance of such measurable environmental factors as hazard, experience, and effort in the maintenance of health in men exposed to their effects. These relationships could then be taken into account in laying down the broad principles of tour limitation.

Outline of Method

In such a study, the effects of these measurable external factors in health and morale were assessed by the varying incidence of neurosis and venereal disease among the flying crews. Men react differently to strain; some find refuge in neurotic illness, while in others the weakening is one of morals rather than of morale. With the monthly incidence of these two types of illness as criterion, then, the relative importance of any environmental factor can be gauged by the closeness of the association between its varying intensity and the fluctuations in the incidence of nervous and venereal disease.

As Bomber Command formed the largest body of men in the R.A.F. engaged in operational flying of a particularly hazardous and strenuous character, the vital and operational statistics of the five major Groups of this Command were studied for a period of twenty months from June, 1943, to January, 1945, inclusive. Product moment coefficients of correlation were calculated between the criteria and various items believed to indicate the magnitude of the several environmental factors of importance. The conventions adopted may be briefly set out.

Criteria of Effects of Stress

Neurosis.—The incidence of psychological disorder is taken as the percentage of the average air crew strength for any month who were referred during that month for psychiatric opinion because of psychological disorder. It might have been preferable to assign these cases to the month in which they became non-effective. As the delay between the latter date and the date of the first psychiatric interview is normally fairly short, however, this should affect the extent rather than the nature of the relationships between the incidence of neurosis and the items investigated. Similarly, it was impossible to account for cases of psychological disorder dealt with on the stations without being referred to the psychiatrist. This, too, may lessen the closeness of the correlation, but it should not hide any striking relationship which does exist.

Venereal Disease.—Similarly, the incidence of venereal disease is taken as the percentage of the average air crew strength reported as fresh cases of venereal disease during the month in question.

Measures of Environmental Factors

Hazard.—The hazard or degree of personal danger to which crews are subject in any month is best measured by the casualty rate through operational causes, i.e. in battle or in flying accidents, in that month. This hazard rate is the percentage of the average monthly crew strength who become casualties during the month. The cumulative effect of hazard is taken into account by calculating the correlation coefficient between the neurosis incidence in one month and the casualty rate both in the same month and in the month before.

An alternative method of measuring the degree of hazard is to calculate the average number of aircraft lost through enemy action in the course of every hundred sorties carried out by the Bomber Group in the month. This percentage has been termed the " missing per sortie " rate. It depends in part, of course, both on the effectiveness of the enemy opposition and on the skill of the crews' defensive tactics. To some extent it is thus a measure of their operational efficiency. It is also a measure of the *rate* at which casualties are occurring rather than the *total* casualties suffered during the month.

Inexperience.—The level of operational experience of the Group is quite easily measured by calculating the percentage of the average crew strength for the month who have been posted into the Group, on completion of training, during the month. In other words, this percentage expresses the proportion of the squadrons' strength who are novices to operational flying.

Effort.—The cumulative effect of long hours of highly skilled activity should be reflected in an association between the incidence of neurosis and features of squadron employment to which fatigue is often attributed. Among these are the average number of flying hours per individual in each month and/or the frequency and average duration of the sorties occurring during that month. The total number of hours, operational and non-operational, flown each month by all the aircraft in the Group, and the average number of men on board being known, it is easy to calculate the mean number of flying hours done by each man in each month. The frequency with which each man operated, i.e. the average number of sorties per man per month, is calculated in the same way from the total number of aircraft sorties carried out by the Group in the month in question. Similarly, the number of operational hours and the number of sorties carried out by the Group in any one month being known, simple division of the former by the latter gives the average duration of sortie during that month. As when dealing with the effect of hazard, the cumulative effect of the operational effort from one month to the next can be gauged by the correlation between the flying time and sortie duration and frequency averages for one month and the incidence of neurosis in the next.

Summary of Results

For security reasons it is unfortunately impossible to give in detail the figures upon which these measures are based, but they derive from the experience of the whole of Bomber Command at a period of its maximum strength. The correlation coefficients indicating the relationship between these measures and the criteria are given in Table I where they are arranged in order of their magnitude under the headings as previously defined.

For venereal disease, similar results were obtained; the only significant correlations were between the venereal disease incidence and the casualty and inexperience groups of items (Table II).

It would appear from these correlation coefficients that only hazard and inexperience are significantly related to the selected criteria of the effects of operation strain. There is no evidence of such a clear relationship between the criteria in the "effort" group of items; yet these items may be fairly termed "fatiguing" in that they might be expected to have a cumulative effect on the mental health of the crews. It is clear that the monthly variation in "effort" in this study has not had an appreciable effect on the monthly incidence of neurosis.

Some allowance must be made for the association between the influx of new crews in any one month and the heavy casualty rate sustained by these operationally inexperienced men in the succeeding month. At the same time, in the latter month, these men reach the critical stage in their tour when breakdown is most likely. The association between the neurosis rate and the casualty rate in any month may therefore be merely an expression of their common relationship to the novice rate in the

TABLE I

Correlation between Items and Neurosis Rate

	r =
A. "*Hazard*" *group of items*	
1. Casualty rate (in same month)	0·4194 xx
2. Casualty rate (in previous month)	0·3312 xx
3. Missing per sortie rate (in previous month)	0·2455 x
4. Missing per sortie rate (in same month)	0·2404 x
B. "*Inexperience*" *group of items*	
1. Novice rate (in same month)	0·2906 xx
2. Novice rate (in previous month)	0·2869 xx
C. "*Effort*" *group of items*	
1. Total flying hours per man (in previous month)	0·1163
2. Total flying hours per man (in same month)	0·1157
3. Average sortie duration (in previous month)	0·0933
4. Average sortie duration (in same month)	0·0351
5. Operational flying hours per man (in previous month)	0·0323
6. Average frequency of sorties per man (in previous month)	0·0267
7. Average frequency of sorties per man (in same month)	0·0029
8. Operational flying hours per man (in same month)	0·0019

xx denotes highly significant relationship, $P < \cdot 01$.
x denotes a significant relationship, $P < \cdot 05$.

TABLE II

CORRELATION BETWEEN OPERATIONAL FACTORS AND V.D. RATE

	r=
A. "*Hazard*" *group of items*	
1. Casualty rate (in previous month)	0·4109 xx
2. Casualty rate (in same month)	0·2972 xx
B. "*Inexperience*" *group of items*	
1. Novice rate (in same month)	0·2399 x
2. Novice rate (in previous month)	0·0350

xx denotes highly significant relationship, $P < \cdot 01$.
x denotes a significant relationship, $P < \cdot 05$.

previous month. Fortunately this possibility can be taken into account by calculating the partial or net correlation between the casualty rate and the neurosis rate in any month when the novice rate in the previous month is kept constant. The value obtained ($r = 0 \cdot 3734$) shows that the casualty rate in any month is significantly more closely associated with the neurosis rate than might be explained by their common relationship to the proportion of inexperienced crews. Similarly, there exists a significant net correlation between the novice rate in any month and the neurosis rate in the next, even after eliminating the effect of simultaneous variations in the casualty rate ($r = 0 \cdot 2044$). The experience in venereal disease is analogous; the net correlation between the casualty rate in one month and the venereal disease rate in the next is, when the novice rate is kept constant, significantly high ($r = 0 \cdot 3546$). On the other hand the net relationship between the novice rate and the venereal disease rate becomes insignificant ($r = 0 \cdot 1292$) when simultaneous fluctuations in the casualty rate are taken into account.

The position may be summarized by suggesting that although correlation, particularly in a time series such as this, does not necessarily mean causation, the hazard of operational flying has both an immediate and delayed effect on the incidence of both neurotic and venereal disease. The immediate effect is most marked on neurotic illness; the delayed effect, probably as the result of the delay in obtaining opportunities for infection and the incubation period of gonorrhoea (the most frequent type), was more definite in venereal disease. Further, the immediate response to the realization of the dangerous nature of their duty was reflected in an increase in neurosis, particularly among the inexperienced men, but the rise in venereal disease was not particularly frequent among operational novices.

PRACTICAL CONSEQUENCES OF RESULTS

Of the measurable environmental factors affecting health and morale, operational hazard is thus clearly of decisive importance. Conversely, factors such as the number of flying hours done by each man and the frequency of operating do not produce the cumulative effect on mental health which conventional ideas about "fatigue" might have led one to expect. In laying down a policy of tour limitation, therefore, the duration of the operational tour to be expected from those who survive long enough to become due for relief must take these facts into account. No arbitrary number of flying hours can be taken as the optimum limit in all types of flying. Since the number of hours flown does not in itself determine the incidence of neurosis, it would be unrealistic to translate a tour limit of x hours from, say, long-range flying boat sea patrols to the conditions of intensive fighter operations. Tour limits may be *expressed* in flying hours, but they had to be framed to take into account the hazard involved in the particular type of flying in question. The basic principle adopted was the setting of the limit at a level giving the individual a chance of surviving the particular hazards entailed which could be faced without breakdown in health and morale by the resolute type of man who elected to serve in the air. Exactly what that limit should have been was difficult to assess. Within the range of casualty rates experienced by Bomber Command during the period reviewed, there appeared to be no point beyond which a sudden serious deterioration took place. The physical measures of health already mentioned gave no indication of a decline in health among those who survived the initial period of adaptation. On the other hand, the hazard of bomber operations was such that the incidence of neurosis in Bomber Command was higher than in any other Command of the Royal Air Force (Symonds and Williams, 1947). The

"expectation of life" prevailing in that Command could, therefore, be taken as a minimum rather than an optimum for general application and the duration of the operational tour in other forms of combat flying set to ensure that the individual pilot had at least the same chance of survival as was general in the bomber offensive against German targets.

Sickness on Sorties: a Specific Enquiry

Useful as these general indications were, the size of the multiple correlation coefficient between neurosis, and hazard and inexperience ($R = 0{\cdot}4585$) suggests that these factors accounted for only about 21 per cent. of the total amount of variance in the incidence of neurosis. They take no heed of intangibles such as squadron leadership and personal morale. Tour limits can be laid down very broadly, but in their application to an individual case the complex of relevant personal and environmental features must be resolved by the squadron commander, aided by his medical officer, in determining the best time of relief from further operational duties.

Typical of the problems met with by the squadron doctor was the case of sickness causing the abandonment or cancellation of an operational sortie. This was an unusual event (it happened about once in every 5,575 person-sorties), so that no single medical officer could acquire the body of clinical experience needed to frame a sound prognostic judgment. Yet, if no obvious physical reason for the sickness was present, two questions rose urgently in the mind of the squadron doctor:

(*a*) Is this sickness likely to be a portent of impending breakdown?

(*b*) Does the return to full duty of this man, whose morale and efficiency may be suspect, entail an increased hazard for the aircraft in which he is flying?

To assess the prognostic significance of the basic patterns of reaction observed, statistical studies were made of a series of such cases occurring in Bomber Command.

Outline of Method

The nature of the two critical questions implies that some follow-up of the subsequent operational careers of the sick men is required. Not only must their own medical and operational histories be obtained and analysed, but a suitable standard of comparison must be afforded. This was effected in practice by making a series of paired comparisons between the "sick" case and a corresponding "control" man selected from among the others in the squadron. From the Squadron Weekly Aircrew List for the week in which the sickness occurred was selected a "pair" for the man whose illness during or just before a sortie had caused its abandonment or cancellation. This "control" man was selected as far as possible so that each pair was comparable in respect of these items in the following order of priority: (1) crew duty; (2) number of sorties performed before the date of the sickness; (3) squadron; (4) officer or non-commissioned officer status. Thus it was hoped to control the influence on morale and efficiency of such factors as the stresses specific to the task in the air, operational experience, squadron leadership, and living conditions. In other words, during their subsequent careers in the squadron, both the "sick" man and his "control" were subject to the same environmental influences and differed only in the one respect of this particular type of sickness. In a group of such pairs, the differences between their subsequent performance should therefore be due mainly to differences in the psychological qualities of the individuals themselves, since both men in each pair are equally likely to be affected by the chances and hazards of flying in war.

The subsequent operational career of each of the men thus paired was followed up through the records of the Personnel Staff sections in each Group Headquarters. Two features were examined in particular:

(1) the cessation of flying duties through illness, whether physical or psychological;

(2) the survival time subsequent to the date of sickness, measured for each man of the pair by the number of sorties completed.

These features were recorded together with all the relevant medical data about the sick case, on cards which could then be sorted into groups. The manner of this division depended on the factor being studied, for example, nature of symptom pattern, previous operational experience, etc. Inter-group as well as inter-pair differences could thus be investigated and the relative prognostic importance of both sickness in general and of some additional factor, such as experience, assessed. The statistical methods involved are detailed in the appropriate tables in each section.

In the clinical assessment of the likelihood of a psychological basis for the complaints which necessitated the return of the aircraft, full weight would be given to definite physical signs of disease; but in so many of these cases no such definite aid is forthcoming and the medical officer must rely upon a subjective account of the symptoms. In order to assay the relative prognostic importance of various

types of symptom pattern, the pairs of sick cases and their controls were divided up on the basis of an arbitrary grouping of the presenting symptoms.

1. *Syncope.*—All cases where the patient lost consciousness were taken separately. These cases were divided into:

(*a*) those where the fainting was clearly due to a failure of the oxygen supply;

(*b*) those where no defect of the oxygen apparatus could be found. Fainting was here usually preceded by dizziness, defective vision, and vomiting, and often followed by stupor.

2. *Nervous.*—Cases in which fainting did not occur but where symptoms referable to the nervous system were complained of, were next classified together. These symptoms fall broadly into two groups, the first dealing with intellectual and emotional disturbance and the second with more specific physical complaints. These grades may be described in more detail:

(*a*) inability to concentrate, lack of confidence in his ability to carry out his duty, frank admissions of panic or fear, feelings of anxiety or acute depression perhaps accompanied by weeping;

(*b*) dizziness, blurring of vision, complaints of confusion, fatigue or "muzziness," faintness without loss of consciousness, neuritic pains, muscular weakness, backache, "pins and needles," sweating and rapid breathing.

3. *Alimentary.*—Nausea, epigastric pain, heartburn, waterbrash, vomiting, colic.

4. *Airsickness.*—Cases were classified as airsickness only when there was a clear previous history of airsickness.

5. *Respiratory* (and ear, nose, and throat).—Painful ears, sinus pains, cough, breathlessness, asthma.

6. *Injuries.*—Usually minor injuries, received just before take off.

In following up the operational careers after the date of sickness, particular note was taken of the reasons for cessation of full flying duties. Medical reasons for becoming non-effective might be physical or psychological. "Psychological reasons" have here been extended to include not only frank neurotic disorder but also executive disposal, for example, on grounds of "lack of moral fibre." The prognostic importance of any feature of the group being studied will therefore be indicated by the disparity between the proportion of subsequent psychological failures in the "sick" and "control" series of paired cases.

Summary of Results

Table III shows the wastage rates for physical and psychological reasons in each of the symptom pattern groups already described.

Inspection of the final percentages in Table III shows that although the wastage for physical reasons in the "sick" group (6·5 per cent.) is larger than in the "controls" (3·2 per cent.), this disparity is not nearly so striking as the difference between the corresponding psychological wastages rates of 23·2 per cent. and 0·6 per cent. Prognostic importance being measured by the extent of this disparity, the syndrome sets can be classified by the size and significance of the difference in psychological wastage rates between the "sick" and "control" group in each syndrome set. Table IV shows how the syndromes may be thus divided into

TABLE III

Physical and Psychological Wastages in Symptom Groups

	No. of Pairs	Physical wastage				Psychological wastage			
		Sick		Control		Sick		Control	
		No.	%	No.	%	No.	%	No.	%
"Syncope"	19	0	0·0	0	0·0	15	78·9	0	0·0
"Nervous"	31	2	6·5	2	6·5	9	29·0	0	0·0
"Alimentary"	47	1	2·1	1	2·1	6	12·8	0	0·0
"Airsickness"	7	0	0·0	1	14·3	1	14·3	0	0·0
"Oxygen lack"	9	0	0·0	0	0·0	2	22·2	1	11·1
"Respiratory"	34	7	20·6	1	2·9	3	8·8	0	0·0
"Injuries"	8	0	0·0	0	0·0	0	0·0	0	0·0
Totals	155	10	6·5	5	3·2	36	23·2	1	0·6

those which are significantly related to the chance of subsequent psychological failure and those where the differences might well be due to chance. Further, the former group may be placed in order of importance by the extent of this disparity.

Table IV shows that although there is a consistent tendency for those who have been sick on a sortie to incur a later psychological disability, this tendency is only significant in three syndrome groups—"syncope," "nervous," and "alimentary"—in that order. It should also be noted that only the first of these is anything like a certain indicator of psychological breakdown. Other features of each individual case, operational experience and time of onset, must therefore be considered as in Tables V and VI.

This division of the cases into groups according to the number of sorties completed prior to the date of sickness shows that the psychological wastage rates rise to a maximum early in the tour, that is, that sickness occurring during the first ten sorties is much more likely to be psychogenic than if it arises later in the tour (a table comparing the numbers of wastages among sick men who had done less than ten sorties and the remainder gives $\chi^2=5{\cdot}0763$, n=1, $\cdot 05 > P > 0{\cdot}02$). This, of course, is in keeping with the previous work which demonstrated the increased effects of stress on the operationally inexperienced.

Similarly, the importance of the stage in the particular sortie at which symptoms arose is evident in Table VI. The original reports of these sicknesses showed not only the time of take-off but also the time of onset of symptoms. The difference between those times thus indicates the stage in the sortie or distance out from base when the symptoms were first observed.

TABLE IV

SYMPTOM PATTERN AND DISPARITY IN PSYCHOLOGICAL WASTAGE RATES

Syndrome type	No. of pairs	Difference %	S.E. of difference %
Significant			
"Syncope" ..	19	78·9	±9·4
"Nervous" ..	31	29·0	±8·2
"Alimentary" ..	47	12·8	±4·9
Not significant			
"Airsickness" ..	7	14·3	*
"Oxygen lack"	9	11·1	*
"Respiratory, etc." ..	34	8·8	±4·9
"Injuries, etc."	8	0·0	±0·0

* Exact treatment of these small samples shows the difference to be insignificant.

TABLE V

INTERRELATION OF OPERATIONAL EXPERIENCE AND SUBSEQUENT HISTORY

Operational experience in sorties	No. of pairs	Psychological wastage			
		Sick		Control	
		No.	%	No.	%
0-3	39	10	25·6	0	0·0
4-9	41	15	36·6	0	0·0
10-19	46	9	19·6	1	2·2
20+	29	2	6·9	0	0·0
Total	155	36	23·2	1	0·7

Table VI shows that although most of the sickness occurs early in the sortie, the chance of subsequent psychological failure rises consistently in each successive stage of the sortie. This suggests (although the χ^2 value of 5·3679, n=2, $\cdot 10 > P > \cdot 05$ is barely technically significant), that illness arising later in the sortie is more likely to have a psychological basis than sickness occurring either at take-off or in the first half-hour. In the previous study on navigator performance it was observed that efficiency fell off as the enemy coast was approached, presumably due to the increasing effects of anticipatory anxiety. It seems likely that this effect is becoming apparent in the increased likelihood of psychogenic upset occurring as the sortie progresses.

All three factors, then, symptom pattern, operational experience, and stage in sortie, are probably related to the likelihood of psychological failure in the subsequent flying career. Despite this association, however, it does not necessarily follow

TABLE VI

TIME OF ONSET AND SUBSEQUENT HISTORY

Stage in sortie (flying time in minutes)	No. of cases	% of total cases	Psychological wastage	
			No.	%
0-9	45	29·0	7	15·6
10-29	20	12·9	3	15·0
30-39	23	14·9	6	26·1
40-59	27	17·4	6	22·2
60-90	27	17·4	9	33·3
90+	13	8·4	5	38·5
Total	155	100·0	36	23·2

that each of these factors can be taken as independent items of clinical evidence in formulating a prognostic judgment. If one factor overlaps much with another, for example if *all* cases of syncope occurred in the later stages of the sorties, then taking stage of sortie into account would not enhance the accuracy of a prognosis based on our experience of syncope cases alone. On the other hand if the two are not related, then one can legitimately consider the stage of sortie as additional information of prognostic value. The contingency tables giving the relationships between each of the three factors are not reproduced, but they suggest that there is no significantly close relationship between them; this is confirmed in each instance by the χ^2 test. It follows, then, that in any individual case the information relevant to each of these three aspects can be combined in framing an estimate of the likely outcome of the patient's subsequent operational career.

The risk entailed in allowing a man who has suffered from a sickness which might well be psychogenic to go back to operational duty can be measured by the difference, if any, in the number of sorties subsequently completed by the "sick" compared with the "control" member of the pair in the same squadron at the same time. Any gross disparity in favour of the controls would imply that the return of the "sick" men to their operational duties entailed an increased hazard for the aircraft in which they flew. The differences actually observed are given in Table VII.

As Table VII indicates, there is a slight adverse difference in the total number of sorties subsequently performed in the group who went on operating even after a sickness of a type normally associated with a liability to psychological failure. The "t" test for the significance of this mean difference between pairs indicates, however, that the difference might easily have occurred by chance. Further subdivision of the cases was hardly justified by the numbers involved, so that it must be concluded from these results that if a man carried on without breakdown after an illness in the air which might well have been psychogenic in origin, his presence in the crew did not seem to affect appreciably the aircraft's chance of safe return in subsequent sorties.

TABLE VII

COMPARISON OF SUBSEQUENT OPERATIONAL SURVIVAL TIME IN SORTIES

	No. of cases	Sorties subsequently completed ("Sick" *v.* "Control")	
		Mean difference	S. error of difference
S.N.A.*	63	−1·35	±1·48
Others	42	+2·14	±1·68

* S.N.A.—"Syncope," "Nervous" and "Alimentary" disorders.

DISCUSSION

These studies are typical of the field research which formed a useful complement to clinical and laboratory work in war medicine. They are important for the confirmation which they gave in this instance to the suggestion that anxiety was more important than prolonged effort as a cause of deterioration in health and operational efficiency. Essentially statistical in methodology, they show how the numerical approach can be a useful adjunct to the clinical or impressionistic methods which rely upon the intuitive judgments of the skilled observer and to laboratory work where realism must so often be sacrificed to technical convenience.

The recognition and measurement of the effects of the mental stresses inherent in the operational environment is important in war; the physical conditions of battle may change, but the principles of action in human behaviour remain. But these methods and results, though useful in war, may be none the less useful in peace. Admittedly we have dealt with the effects of particularly severe strains on a highly selected group, but the principles probably hold for the results in the less resilient population of a factory of the far from negligible emotional stresses of industrial life. The many-sided aspect of the reaction to stress—the failing efficiency, the objective signs of physical deterioration, and the characteristic symptom patterns—calls for an equally varied taste in the methods used in such studies.

If Service experience such as here described be taken as a guide, it would appear that the convergent attack on a single problem by workers skilled in clinical, laboratory, and statistical field research is a useful approach to the difficulties of investigation in social medicine.

SUMMARY

This paper describes typical field studies, carried out in Bomber Command of the Royal Air Force during the war 1939-45, on the effects of operational stresses both on the incidence of certain diseases and in individual cases of sickness occurring in the course of bomber operational sorties.

A study of the relationship between the incidence of neurosis and venereal disease and various indices of operational hazard and effort suggests that the acute anxiety caused by a high casualty rate had a

much more decisive effect on health and morale than had prolonged or intensive operational effort.

Operational inexperience which also plays a part in determining the incidence of neurosis, is shown to be relevant in the prognosis of cases of sickness occurring in conditions of acute stress on operational sorties. The chance of subsequent psychological failure in such cases is also seen to have been related to the type of presenting syndrome and the stage in the sortie at which the sickness appeared. Fainting and symptoms referable to the nervous and alimentary systems, particularly if they arose some time after take-off, were indicative of impending breakdown. In those instances where this did not occur, however, no extra risks to the aircraft in which he flew were incurred by allowing the man to continue on operational duty.

These suggestions of the predominant effects of anxiety over "fatigue" (in the sense of the end results of prolonged effort) can be related to the findings of laboratory and clinical research done in the Royal Air Force. The value of simple statistical methods in field research as a complement to laboratory and clinical studies is discussed.

I am indebted to Air Marshal Sir Harold Whittingham, Director General of Medical Services of the Royal Air Force during the war, for his encouragement, to the Consultants in Neuropsychiatry and Medical Statistics, Sir Charles Symonds and Prof. A. Bradford Hill for their direction and advice, and to the present Director General of Medical Services, Royal Air Force, Air Marshal P. C. Livingston, for permission to publish this work. My thanks are also due to Miss G. M. Penfold, formerly Corporal W.A.A.F., for secretarial and computing assistance.

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THE GERONTOLOGICAL ASPECTS OF ATHEROMA
AN APPROACH TO A PATHOLOGY OF SENESCENCE

BY

ERICH GEIRINGER*

From the Edinburgh Gerontological Research Unit, Usher Institute, University of Edinburgh

We may, as a matter of convenience, distinguish two categories of gerontological research, the study of old age or old people on the one hand, and the study of ageing on the other. Almost the whole of pathology is our field in the study of old age; for whilst there are very few diseases which spare the aged, many present special features when occurring in them, either attacking them more readily or being more dangerous and less tractable. The study of these phenomena presents a vast and important task, in which, however, orthodox pathology can be of great help. In the study of ageing the field is much narrower and the guidance to be derived from existing disciplines much less.

Each one of the diseases of old age is characterized by the fact that it attacks individuals or groups of individuals, leaving a significant proportion of mankind untouched. These diseases are, however, only the superimposed complications of an underlying process of functional deterioration in which all human beings share, and it is with this universal process that we are concerned in the study of ageing.

It must be admitted that strict proof for the existence of such a separate process of ageing is lacking. The concept that we are all subject to an identical process or complex of processes of deterioration is based on purely circumstantial evidence and on an impression which has been prevailing in the human race throughout the centuries. But if, as a working hypothesis, we accept the existence of ageing as a separate physiological or pathological entity and begin to look round for its manifestations, we are struck by the extraordinary difficulty of finding them. In order to be acceptable as a part of the complex of senescence a phenomenon must fulfil at least two conditions: it must be exhibited by *all* the members of the species, and it must be demonstrable at a time at which the complications of old age are still rare.

Atheroma of the aorta is one of the very few conditions which not only passes the test of both these criteria but also furnishes us with easily accessible and comparatively easily measurable lesions. An analysis of aortic atheroma might, therefore, apart from its intrinsic interest, contribute to our understanding of the process of senescence.

Method

At autopsy the aorta was removed together with the iliac arteries and the main pulmonary trunk. It was stored in 10 per cent. formol. At a later date it was divided into eight strips, in each of which the extent and severity of atheroma was graded according to an arbitrary numerical scale. The arithmetic mean of the eight results constitutes the total grade of the vessel. At the same time a verbal description of the appearances was written down. Each aorta is identified by a number only, and the grading was carried out in complete ignorance of the clinical and pathological findings in the case. Bias was thereby excluded except perhaps in the few instances in which a peculiarity of the vessel called the circumstances of the case to mind. Equally, the classification of the clinical and pathological conditions in each case was carried out without knowledge of the state of the aorta, and the two records were only brought together when both the grading of the vessel and the clinico-pathological classification of the case had been completed. The fact that all these investigations were carried out by one individual probably serves to enhance the consistency of the results.

The criteria used in determining whether hypertension had been present were in the first place the clinical records and then the absolute and relative heart weight and the state of the renal arterioles. There are many sources of error in each one of these criteria, and not only were the whole of the other findings taken into consideration (with the exception of course of the state of the aorta), but no case was classified as either a proved hypertensive or a proved normotensive in which any one of the above criteria allowed of any doubt. Whilst this resulted in a low number of such classifications it is felt that the increased reliability of the individual correlations more than compensates for the loss in statistical significance.

* Whaitt Research Scholar.

The Frequency of Atheromatous Involvement

A study, in this manner, of three hundred autopsies has confirmed the observation of Zinserling (1925) and others that *atheroma of the human aorta* becomes very frequent after the age of 6 months and *is invariably present after the age of 8 years.* In Fig. 1 which shows the extent of atheromatous involvement of 180 aortae, it can be seen that the zero-line is completely unoccupied.

This fact has never been given sufficient emphasis. To the histo-pathologist it cannot be of great importance; from a gerontological point of view, however, this 100 per cent. incidence (which has been confirmed in places as distant from one another as Switzerland (Saltykow), Russia (Zinserling), Germany (Lubarsch), and Scotland and at dates as widely separated as 1913, 1919, 1925, and 1948) is highly significant. It entitles us to regard atheroma aortae as a racial characteristic of *homo sapiens*, a part, we might say, of the "normal pathology" of man.

Pathogenesis of Atheroma

The uncertainty which still prevails about the motor causes, the pathogenesis, of atheroma has lately tended to obscure the fact that we are perfectly familiar with its final exciting cause, which is the action of arterial blood pressure upon the aortic wall. This well substantiated fact is explicitly or implicitly recognized in all the important work in this field. To put the matter in a nutshell: *the human aorta is neither adapted nor completely adaptable to the human aortic blood pressure.*

From the time of onset of atherogenesis, and from other lines of evidence such as is offered by a study of atheroma of the pulmonary artery, we are even enabled to put an approximate value upon the critical pressure above which atheroma will make its appearance. It is about 50 mm. Hg. How pressure brings about this effect is an important question:

whether by dragging upon fixed points of the vessel wall (Duguid),

whether by traumatizing the intima and leading to intimal haemorrhage (Winternitz) or mural thrombosis (Duguid),

whether by causing a pressure ischaemia with subsequent degeneration of the intima (Moon),

whether by upsetting the colloid balance of blood cholesterol (Anitschkow),

whether by the opening up, in the endothelium, of stomata through which an excess of blood-lipoids is passed (Leary, Lange),

whether by producing shearing strains between vessel wall and blood stream (Allbutt),

whether by inducing intimal herniation (Krafka),

whether by weakening the media with subsequent dilatation and consequent compensatory proliferation (Thoma),

whether by loosening the ground substance and allowing the infiltration of plasma constituents (Virchow, Aschoff).

The Pathogenic Action of Normal Function

These theories are, however, not relevant to our present purpose. They all have a common aetiological background, viz. *the action of normal blood pressure upon the normal aortic wall.* This is of considerable gerontological interest because it furnishes us with an example of the "*pathogenetic action of normal function,*" of which we shall meet many more by and by in the study of ageing if the concept of senescence as a separate entity has any validity at all.

It is repugnant to our teleological instincts and to our Darwinian upbringing to look upon normal function as a pathogen. A glance at Fig. 1 helps us in this perplexity. The grades of atheromatous involvement are there characterized by the terms:

Minimal:	from 0 to 1
Mild:	from 1 to 2
Moderate:	from 2 to 3
Marked:	from 3 to 4
Severe:	from 4 to 5

Atheromatous lesions of the first two grades are certainly without any clinical importance. It can be seen that atheroma does not, in the vast majority of cases, assume clinically significant proportions until well after the end of the natural period of reproduction. It does not, therefore, interfere with the survival of the species, and it does not, therefore, tend to become eliminated by natural selection. This, too, is a principle which may have a larger application, and I am tempted to suggest that an adequate definition of senescence might be that it is the sum-total of those inherited flaws in animal organization which become manifest only in the post-reproductive period and therefore show no tendency to become eliminated by natural selection.

The Susceptibility of the Aorta to Atheroma

Study of Fig. 1 also preserves us from the common mistake of trying to explain atheroma by the action of one single factor. The two main features which point to the presence of another factor or factors are first, the continued rise in the severity of atheroma

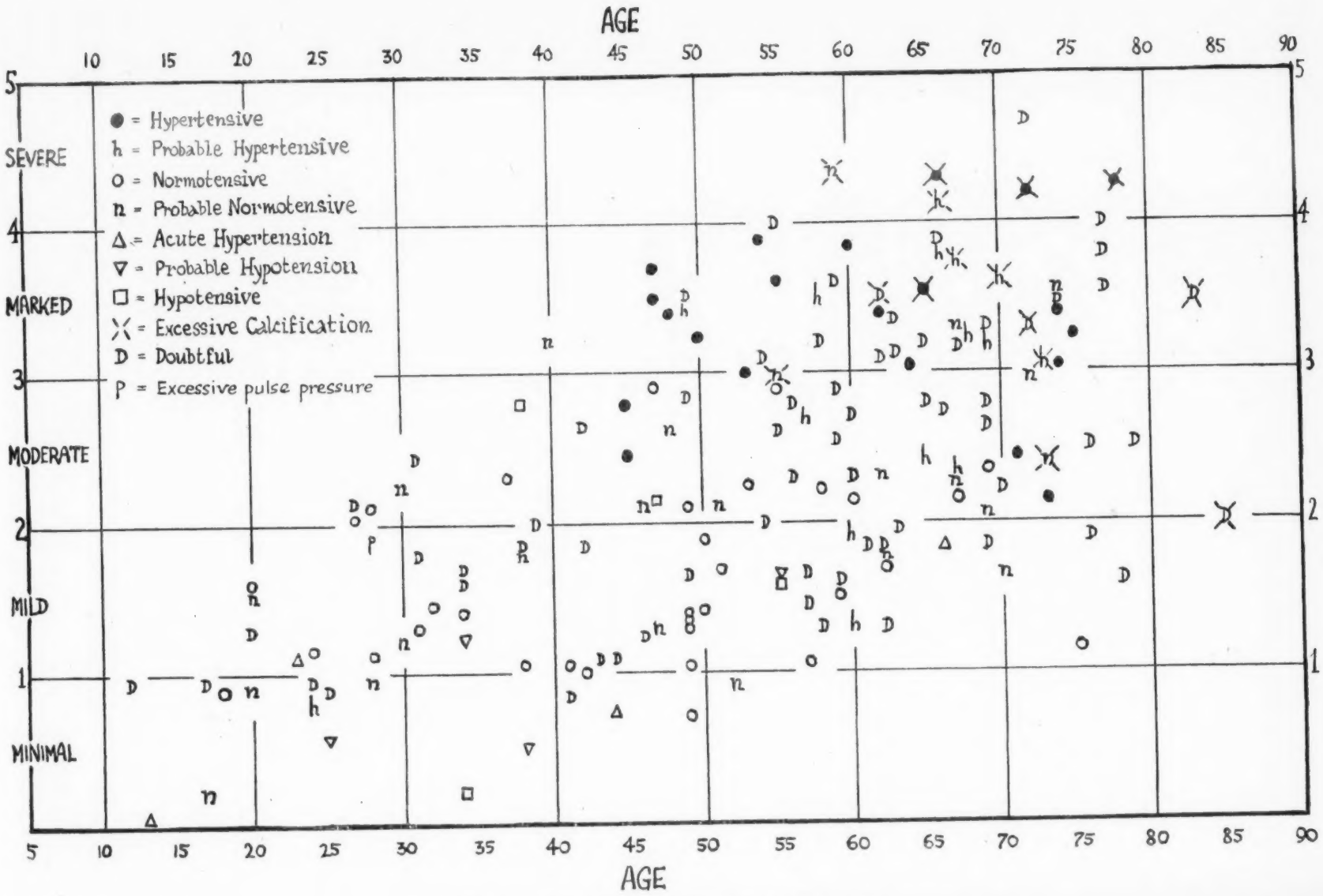

FIG. 1.—Total extent of atheroma in 180 aortae.

AGE

FIG. 1.—Total extent of atheroma in 180 aortae.

ven in the most favourable cases *after* the time at hich blood pressure becomes stabilized, and, econdly, the existence of scatter amongst normo-nsives of the same age. Any attempt to define ese additional factors more closely would lead us once into the pathogenetic battlefield, and we hall therefore be content to refer to these further ausal conditions as " the susceptibility of the aorta atheroma." We might then say that in the resence of a stable exciting cause the susceptibility of the aorta to atheroma increases gradually with ounting age and differs in different individuals at he same age. Recognition of these two factors llows us to form a rational idea of the nature of theroma and resolves many of the apparent radoxes of this condition. Susceptibility may be ormal or increased, pressure may be normal, creased, or decreased; and it is the combination each individual case which determines the extent nd severity of atheroma.

The Behaviour of the Aortic Atheroma in Hypotensive Cases

Of particular interest in this connexion is the behaviour aortic atheroma in hypotensive cases. At first ought we would expect abnormally low arterial pressure be associated with an unusually mild degree of heromatous involvement. This does in fact often tain, as in the case of a woman of 34 (represented in g. 1) who had lingered on for two years, suffering from alignant cachexia and undergoing in that space of time o major operations (average blood pressure in the last ree months of life: 98/68; total extent of aortic heroma: 0·18). In such cases we may see the result the interaction of average aortic susceptibility with an citing force of low intensity. More commonly the ness which induces hypotension interferes at the same me and to a commensurate degree with the reactivity nd adaptability of the vascular parietes. Such a case, woman of 47 (with chronic pulmonary tuberculosis and ddison's disease) is represented in Fig. 1. The extent atheroma in these circumstances is about average for e age-group of the case. Lastly we have to consider nditions in which the interference with the reactivity the tissues exceeds the hypotensive effect. Severe ric diphtheria not uncommonly furnishes examples of is kind, and here extensive atheroma may be the result a pressure considerably below normal. Such cases ay be properly regarded as " relative hypertension," concept of wide applicability in vascular pathology, e imperfect understanding of which has led in the past the enunciation of the various " toxic " theories of e aetiology of atheroma.

Having taken due note of these three different types of potensive case we must in their analysis remember one rther important detail, viz. that the hypotensive state usually only a secondary one, obtaining often only for e last few months of life. Whilst we possess evidence suggesting that purely lipoid plaques may be resolved fairly quickly, it is obvious that fibrous lesions will still persist from the previous normotensive or hypertensive period. A striking confirmation that this last consideration is valid was obtained from a study of the verbal descriptions which are attached to each aortic grading. In describing the atheromatous lesions such terms as " purely lipoid," " predominantly lipoid," " fibro-lipoid " and " lipoid and fibrous " recur constantly. In two cases only the terms used were " almost entirely fibrous " and " mostly fibrous." Both these turned out to be cases of hypotension (a woman of 47 with Addison's disease, and a man of 55 with tuberculosis, mitral stenosis, and emphysema). This certainly suggests that hypotension may lead to an arrest in the new formation of atheromatous plaques whilst the old fibrous lesions persist (lipoid plaques already present undergoing either fibrosis or resorbtion). Unless this point is kept in mind a misleading picture of the relation between hypotension and atheroma might be arrived at.

Severity of Atheroma

In spite of this continuous rise as age advances, it can be seen from the base-line of Fig. 1, which represents the most favourable cases, and from the vast majority of the individual normotensive cases that, right up to the age of 80, atheroma of the aorta remains a trivial complaint; an important fact, since the extent of aortic atheroma is a reliable index of the extent of atheroma in the coronary and in the cerebral vessels (Fig. 2). The hump of marked

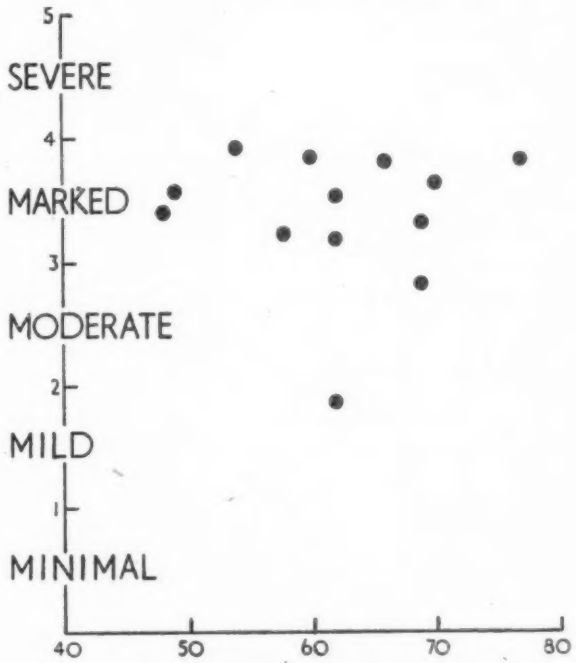

FIG. 2.—Extent of aortic atheroma in coronary thrombosis.

and severe atheroma seen in Fig. 1 between the ages of 40 and 80 is largely made up of cases of hypertension, in other words of cases in which the normal age changes of the aorta have become unduly pronounced by the superimposition of a complicating factor. In this we may see a further characteristic of many of the changes of senescence. They are in themselves trivial and in no way threatening to life, but they form the basis on which dangerous complications arise. Ageing puts us at a disadvantage slight in itself but sufficient to tip the balance against us in our fight with our environmental and constitutional enemies.

If we were to prolong the base line to the right, a purely speculative exercise, we would see that atheroma need not reach a clinically significant level until the age of 140 and not a dangerous level until the age of about 170. Of the complications which interrupt this peaceful ascent towards patriarchal heights we shall first consider hypertension.

Hypertension

From whatever cause it may arise, hypertension almost invariably results in a great increase in the extent and severity of atheroma except wh occurring before the age of 20, when the adaptabil of the aortic wall is often great enough to preve such an increase. In this series a very clear-c division could be demonstrated between the aor involvement in cases with normal blood pressu and in those suffering from hypertension. Whi the two groups share the region of modera atheroma to some extent, *no proved normotens was found in the region of marked or severe atherom and no proved hypertensive in the region of minim or mild atheroma* (Fig. 3). The correlation betwe severe arteriosclerosis and hypertension has impressed some authors that they consider hyp tension to be the cause of atheroma (Moschcowi 1930). In view of the universal occurrence atheroma from an early age, this conclusion patently untenable unless indeed we widen t meaning of the term " hypertension " to inclu any degree of pressure which has a deleterious effe upon the arterial wall. Such a pressure, if with the normal limits for the age group of the case, however, better referred to as a " relative hyp tension," a concept to which allusion has alrea

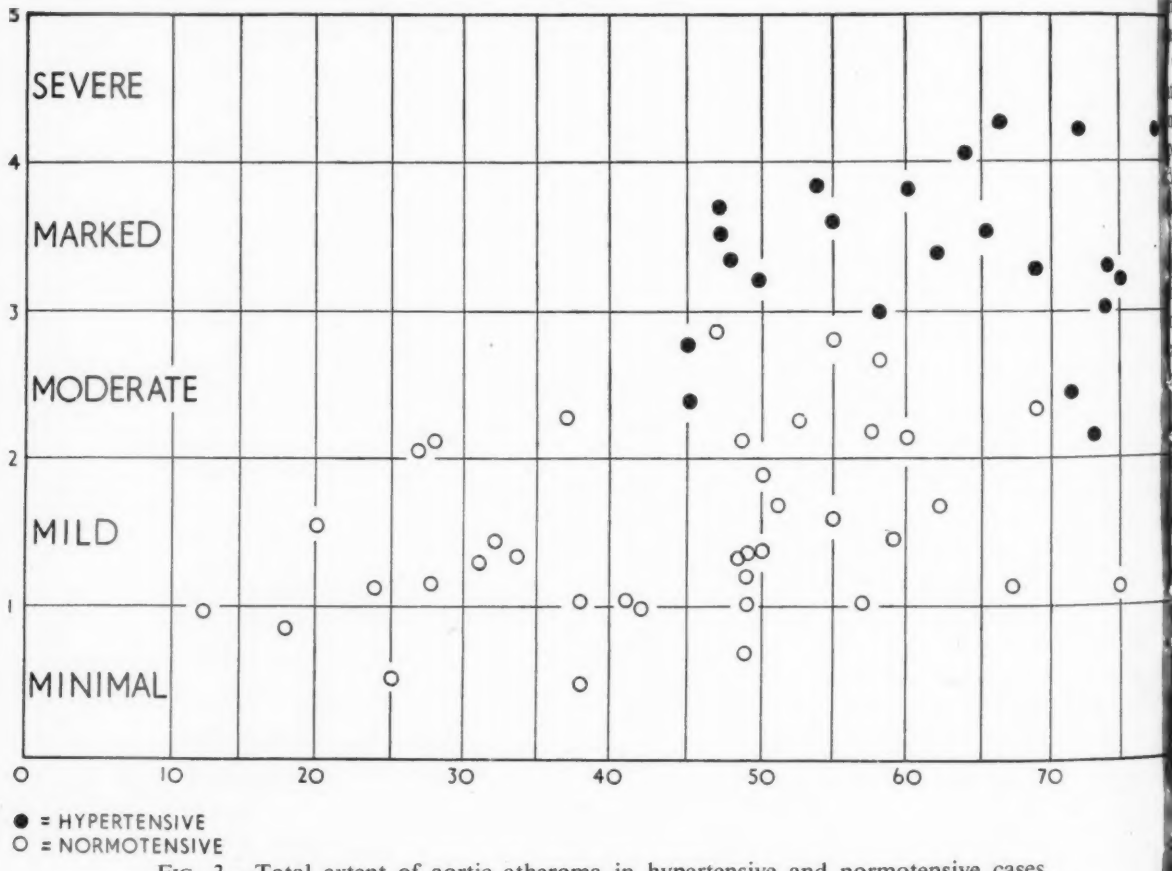

Fig. 3.—Total extent of aortic atheroma in hypertensive and normotensive cases.

en made. Hypertension is a very quent finding in diabetics, and it s therefore thought of interest to mpare the degree of aortic atheroma ases of diabetics with normal blood ssure with that of hypertensive betics. Fig. 4 shows that diabetics h normal blood pressure are no re severely affected than non-betic normotensive subjects. It uld appear, therefore, that the quent association of diabetes with ere atheroma is not a function of diabetes itself but rather one of hypertension which accompanies o often and which even in the n-diabetic leads to an aggravation atheroma.

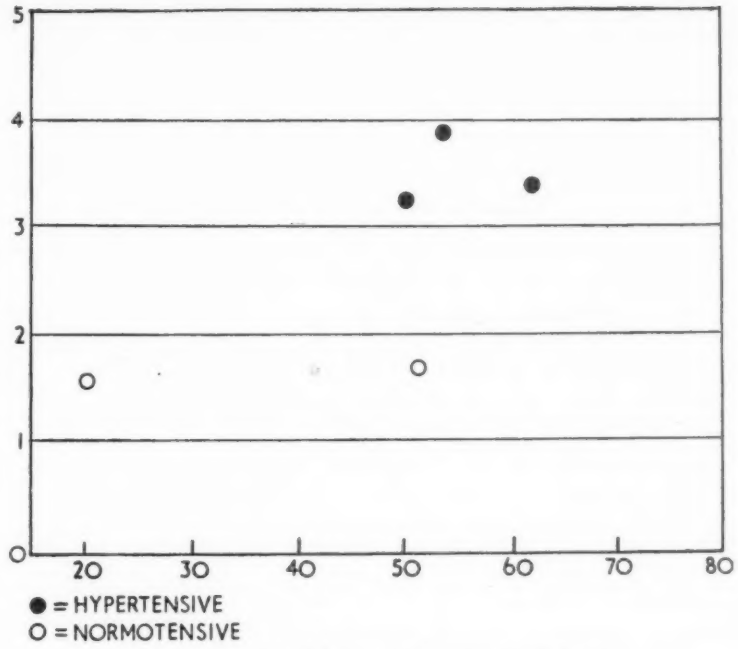

FIG. 4.—Extent of aortic atheroma in diabetics.

CALCIFICATION

Whilst hypertension as a com-ation of atheroma is met with tively early in life, there is ther complication which trans-ms this benign manifestation of escence into a dangerous disease and which very infrequent before the age of 60, and t is excessive calcification. Pathological collec-ns of lipoid material are apt to have calcium posited in them, and it would be very difficult ced to find an aorta after the age of 30 in which roscopic examination would not reveal calcium ome at least of the more chronic plaques. In majority of instances, however, these calcifica-s are discrete and the vessel remains pliable. m the age of 60 onwards there occur with reasing frequency cases of so-called "egg-shell ta," in which excessive calcium deposition in the romatous lesions transforms wide stretches of vessel into a rigid tube. That this is not simply final stage in the natural evolution of atheroma dicated by the fact that very extensive atheroma be found at high ages without gross calcifica-n. The natural end stage of atheroma is fibrosis, the occurrence of excessive calcification in some s points to the intervention in these cases of an itional factor.

Metastatic calcification may be induced experi-tally with considerable ease by the administra-of agents like vitamin D or parathyroid mone, and any tendency to metastatic calcifica-so induced will show its first effects in locations re lipoid accumulations or necrosis facilitate the sition of calcium. We know also of various taneously occurring diseases which act in the same way. Further, a halisteresis of the skeleton is common in old people and may be supposed to be caused by or be the cause of a disturbance of calcium metabolism.

It is therefore likely that, instead of looking upon cases of "egg-shell aorta" merely as cases of severely calcified atheroma, it might be more correct to see in them cases of atheroma complicated by some disturbance of calcium metabolism.

With this possibility in mind, the case notes of the fifteen aortae in which calcification had been graded either as marked or severe were subjected to a careful analysis. That ten of the fifteen are hypertensives is not surprising, since calcification of the extensive atheroma of hypertension is more likely to become graded as severe than the calcification of sporadic lesions. For the same reason the finding of twelve cases of nephrosclerosis among the fifteen is perhaps not startling, but we remember in this connexion the important role which the kidney plays in regulating calcium metabolism as an organ of excretion and, more important perhaps, as a stabilizer of the *p*H of the blood. Ten of the fifteen cases showed major pathology of the gastro-intestinal tract. Nine cases had evidence of metastatic calcification elsewhere, a very high proportion when it is remembered that this analysis was carried out in retrospect. The most striking finding, however, and one which was quite unexpected, was that no less than seven of these fifteen cases showed gross thyroid pathology: one case of myxoedema, one of past thyroidectomy for Graves's disease, two cystic nodular goitres, one smooth colloid goitre, and two cases with large cysts in one lobe—an

incidence ten times that obtaining in the remainder of the present series. These fifteen cases thus form a group representing metastatic calcification plus renal, gastro-intestinal, and thyroid dysfunction in varying combination.

A clinico-pathological investigation is now in progress to elucidate the exact significance of these findings, but meanwhile they seem to underline the fact that cases of excessively calcified atheroma are not just cases that have progressed one stage further along the normal path of evolution of atheromatous lesions but are rather cases of atheroma *plus* a complicating factor.

A clear recognition of this relationship (with which probably few pathologists would be disposed to quarrel) is of considerable theoretical importance. As long as authors persist in classifying excessively calcified atheroma as " severe atheroma " they will continue to point to certain paradoxes which make an understanding of the nature of atheroma difficult. In Fig. 1, for example, we can see the case of a woman, 59 years old, in whom evidence points to the probability that her blood pressure was normal. She takes her place at the top of the chart surrounded entirely by hypertensives. Her case, regarded as one of severe atheroma, would tend to throw doubt on the correlation between height of blood pressure and severity of atheroma. Regarded as a case of atheroma with severe metastatic calcification superimposed, this difficulty vanishes.

But the realization that *excessively calcified atheroma is complicated atheroma* has also some practical importance, for this is a lesion which can often be diagnosed *intra vitam* by radiograph. It would seem important in handling such cases to remember that we are not dealing merely with an individual suffering from severe arteriosclerosis but that there is probably some upset of calcium metabolism as well.

These two major complications of atheroma are at the same time representative of two distinct types of condition which are met with in aged persons. Hypertension acts on the same function from which the basic change is derived and, by increasing the intensity of the exciting factor, leads to an aggravation of the atheroma and to its reaching prematurely a severity appropriate to a later age. We can readily think of parallel phenomena in other parts of the body. For example, the elasticity of lung tissue decreases with advancing age. There is, however, a group of individuals in whom this change occurs prematurely and to an exaggerated degree, leading to clinical emphysema in middle life. Such co plications of ageing are, in their effect, pur quantitative ones.

Excessive calcification exemplifies the othe qualitative—type of complication. Here the ba condition is actually transformed in its nature by extraneous factor which interacts with it—in t instance by a disturbance of calcium metaboli which transforms the lipoid plaque (which otherw might go on to fibrosis) into a calcareous one. terms of the aged lung this could perhaps be likene to infection which so readily supervenes in it transforming the senile emphysema into bronch pneumonia.

Summary

A study of three hundred aortae and a detail analysis of 180 of them reveals the following point

1. *Atheroma of the aorta is invariably prese after the age of 8.* It is therefore to be regarded a racial characteristic of mankind unless and until can be shown to be due to an extraneous and on temporarily active factor.

2. *Atheroma of the aorta is due to the effect normal blood pressure on the normal aortic wa* thus furnishing an example of *the pathogene action of normal function.*

3. *Clinically significant lesions do not as a r occur before the age of 30,* which explains how t defect in our organization has escaped the correcti action of natural selection.

4. *Even after the age of 30,* **uncomplicated** *atheron is a mild and trivial condition,* increasing only ve gradually in severity as age advances.

5. *It provides, however, a favourable soil on wh complications arise* in a great number of cas transforming it from a harmless into a dangero and often deadly disease.

6. *The two major complicating conditions atheroma are hypertension and excessive calcificatio*

In all these features we discern a distinct pattern of pathological behaviour which I belie to be characteristic of the phenomena of hum senescence.

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AN APPLICATION TO A LABORATORY PROBLEM OF DISCRIMINANT FUNCTION ANALYSIS INVOLVING MORE THAN TWO GROUPS

BY

R. F. JENNISON, J. B. PENFOLD, and J. A. FRASER ROBERTS

From the Research Department, Royal Eastern Counties Institution, Colchester, and the Pathology Laboratory, Essex County Hospital, Colchester

We have recently attempted to assess the value of a modification of the Wassermann reaction, based upon the suggestion of Richardson (1940). The results are being described in a pathological journal (Jennison, Penfold, and Roberts, 1949). The present paper deals with certain points which emerged during the statistical analysis, and which have a rather more general interest in regard to the application of statistical methods to biological data.

Material and Methods

The technique for the standard Wassermann test was that described by Panton and Marrack (1945). Three tubes were made up as follows:

Tube	Serum c.cm.	Saline c.cm.	Complement (3 M.H.D. in 0·5 c.cm.) c.cm.	Antigen c.cm.	Sensitized cells c.cm.
1	0·1	0·4	0·5	0·5	1·0
2	0·1	0·2	0·7	0·5	1·0
3 (control)	0·2	0·8	0·5	0	1·0
(4	0·2	0·3	0·5	0·5 diluted 1 in 7	1·0)

Absence of haemolysis in tubes 1 and 2 indicates a positive result; complete haemolysis in both tubes a negative result; partial haemolysis in either or both a doubtful result. Richardson's suggested modification is very briefly this: excess of antigen as in the usual Wassermann reaction does not provide the optimum proportions of antigen and antibody for the fixation of complement; suitable dilution of the antigen gives a proportion nearer the optimum in syphilis, while the non-specific antigens are diluted, usually beyond the point at which they will give their least reaction. In these circumstances the fixation increases (less haemolysis) with syphilitic and decreases (more haemolysis) with non-specific sera, thereby increasing respectively the sensitivity and specificity of the test. Accordingly in the modified technique a fourth tube was added as shown above. Theory would suggest that when the amount of haemolysis in tube 4 was less than or equal to that in tube 1 the result is likely to be positive; when greater than in tube 1 probably negative.

In order to assess the value of the addition of tube 4, 1,000 sera were chosen for the modified test out of some 9,000 routine Wassermann and Kahn reactions. These were deliberately selected as difficult sera:

1. Those showing incomplete fixation with 3 M.H.D. of complement.

2. Those showing a discrepancy between Wassermann and Kahn reactions.

3. Those from treated cases which had not been consistently negative previously with the modified test.

4. Those from cases giving positive routine Wassermann or Kahn reactions, but with no clinical evidence of syphilis.

5. Those from antenatal clinics giving a positive or doubtful presumptive Kahn reaction.

The 1,000 sera were classified into four clinical groups:

Group I. Untreated syphilis.

Group II. Treated syphilis.

Group III. Probable or possible syphilis, i.e. some history or physical signs of the disease.

Group IV. No history or signs of syphilis.

The four groups should thus represent decreasing proportions of true sero-positive syphilis and the criterion against which the technique is assessed is its success in differentiating between them.

Where haemolysis in any tube was partial, its amount was measured to the nearest 10 per cent.

Results

The results for the 1,000 sera by the standard technique, not using tube 4, are shown in Table I Including now the additional information given by

the readings in tube 4, of the 646 sera with complete haemolysis in tubes 1 and 2, 546 also gave complete haemolysis in tube 4, while 100 showed partial haemolysis or no haemolysis. The distribution of the 646 sera between the groups is shown in Table II.

TABLE I

RESULTS OF THE STANDARD WASSERMANN TECHNIQUE

	NUMBERS				
	Group				
	I	II	III	IV	Total
Positive	44	95	20	3	162
Doubtful	13	137	23	19	192
Negative	11	299	97	239	646
Total	68	531	140	261	1,000
	PERCENTAGES				
	Group				
	I	II	III	IV	
Positive	65	18	14	1	
Doubtful	19	26	17	7	
Negative	16	56	69	92	
	100	100	100	100	

TABLE II

RESULTS GIVEN BY TUBE 4 WITH 646 SERA NEGATIVE BY TUBES 1 AND 2

Group	Number	Also negative in Tube 4	Partial or no haemolysis in Tube 4	Per cent. with partial or no haemolysis in Tube 4
I	11	5	6	54·5
II	299	216	83	27·8
III	97	88	9	9·3
IV	239	237	2	0·8
Totals	646	546	100	

This result is a striking one. It is clear that fixation, complete or partial, in tube 4, when there has been complete haemolysis in tubes 1 and 2, does strongly suggest a positive serum; tube 4 has thus undoubtedly improved the sensitivity of the test.

As shown in Table I, 192 sera gave partial haemolysis in tube 1, or 2, or both. Their distribution in relation to tube 4 is shown in Table III, distinguishing those in which haemolysis in tube 4 was less than or equal to that in tube 1 from those in which it was greater. This is also a striking result. Haemolysis in tube 4 which is less than or equal to that in tube 1 suggests a positive serum; haemolysis in tube 4 which is greater than in tube 1 a negative serum; tube 4 has thus undoubtedly improved the specificity of the test.

TABLE III

RESULTS GIVEN BY TUBE 4 WITH 192 SERA DOUBTFUL BY TUBES 1 AND 2

Group	Numbers			Percentages	
	Haemolysis $4 \leqslant 1$	Haemolysis $4 > 1$	Total	Haemolysis $4 \leqslant 1$	Haemolysis $4 > 1$
I	13	0	13	100	0
II	111	26	137	81	19
III	14	9	23	61	39
IV	3	16	19	16	84
Total	141	51	192		

Only 5 sera previously positive, i.e. with no haemolysis in tubes 1 or 2, showed partial haemolysis in tube 4. Three of these sera belonged to group II and two to group III.

It will be noted that the application of the simple rule of taking the difference between the readings in tubes 1 and 4 applies equally to the sera of Table II and of Table III, though it does make the 5 previous full positives "probably negative." There might be, however, an element of artificiality in applying the rule to the 105 previous full positives or full negatives; for with the full positives any haemolysis, however slight, must indicate "probably negative," while with the previous full negatives any fixation, however slight, must indicate "probably positive." Nevertheless, it is clear that a straightforward and very simple deduction from theory does lead to a considerable measure of useful discrimination, judged, as always, by the proportions in the four clinical groups, with their decreasing proportion of true sero-positive syphilis.

FURTHER STATISTICAL ANALYSIS

It seemed profitable to examine the data further, and without preconception, in order to see whether the actual readings in the three tubes could be used in such a way as to secure improved discrimination between the clinical groups. The data are now the 297 (100+192+5) sera in which there was partial haemolysis in one or more tubes, for it seems better not to complicate the analysis with the remaining

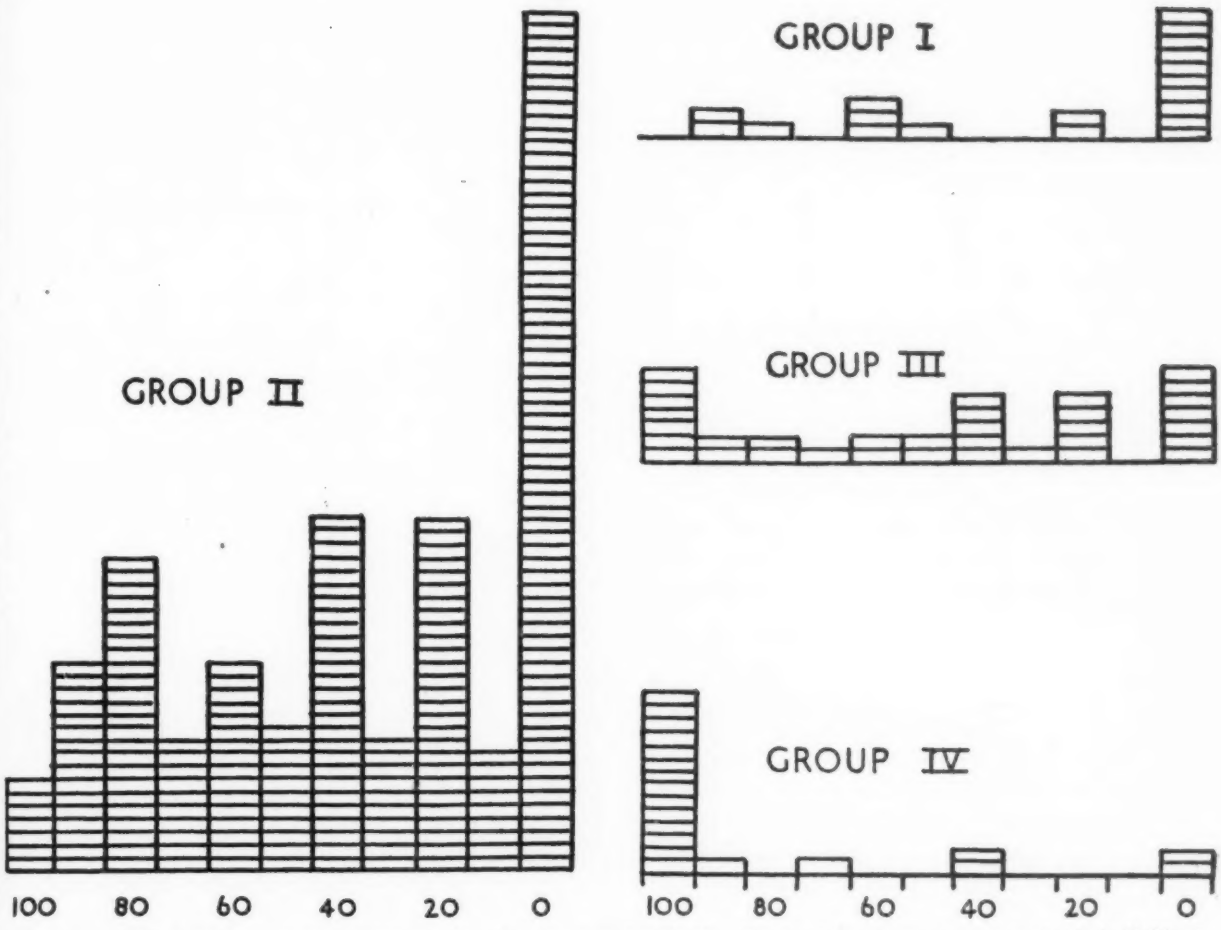

FIG. 1.—Tube 4 only—per cent. haemolysis. Variance ratio 12·10. Each rectangle represents a single individual.

TABLE IV

ANALYSIS OF VARIANCE: MEAN SQUARES AND CROSS PRODUCTS

Variation	Degrees of Freedom	1^2	2^2	4^2	1·2	1·4	2·4	X^2	X_1^2	D^2
Between groups ..	3	5·147	6·165	138·029	−0·537	−6·778	28·076	387·739	380·239	156·732
Within groups ..	293	14·686	8·464	11·410	8·168	5·706	3·655	22·948	22·671	14·684
Variance ratio ..		<1	<1	12·10				16·90	16·77	10·67

X^2 = discriminant function; X_1^2 = rounded off function; D^2 = difference, tubes 1 and 4.

703 which are either fully positive or fully negative in all tubes. The basic data are given in the Appendix Tables. Looking first at the haemolysis readings in the three tubes separately, we find:

	Mean haemolysis (per cent.)		
	Tube 1	Tube 2	Tube 4
Group 1	55·3	78·4	27·9
Group 2	63·7	81·6	37·1
Group 3	62·6	85·6	48·8
Group 4	59·0	89·5	80·5

The percentage readings in tubes 1 and 2 are useless for the further classification of doubtful sera. In tube 1 the means are not even in the right order; in tube 2 the differences are too small to be of any value. In terms of the analysis of variance shown in Table IV, with both tubes the mean square between groups is less than the mean square within groups. The result with tube 4 is very different, the variance ratio of Table IV being no less than 12·10. Actually this is a better result than that given by the difference method of the previous section, which yields the somewhat lower variance ratio of 10·67. Doubtful sera would be rather more efficiently classified by using the figure for percentage haemolysis in tube 4 instead of the difference between tubes 1 and 4.

Although tubes 1 and 2 taken alone provide no useful discrimination, it remains possible that some appropriate combination of all three readings might give better discrimination than tube 4 alone. In the analysis there are four groups. The theory of discriminant function analysis with more than two groups was elucidated by Fisher (1938, 1940), though not very much use seems to have been made up to the present of a method which must have applications in a wide variety of biological problems. The subject is fully discussed, with numerical examples, in a forthcoming book by Prof. K. Mather (1949), to whom we are greatly indebted for showing us the typescript of the section appropriate to our problem.

It is clear that what is required is a single function, for the differences between the four clinical groups are quantitative; we need, therefore, that combination of the three variables which maximizes the difference between groups relative to the variation within groups. The computation involves little more than the evaluation of a determinant of order corresponding to the number of variables. It would, of course, be possible in the present problem to reduce the groups to two by, say, combining groups I and II and omitting group III. But this means losing information, and could not be done at all in many problems to which the method is applicable, and in which the number of groups is indefinitely large: for example, if it were desired to obtain a function which maximized the variation between sibships relative to that within sibships.

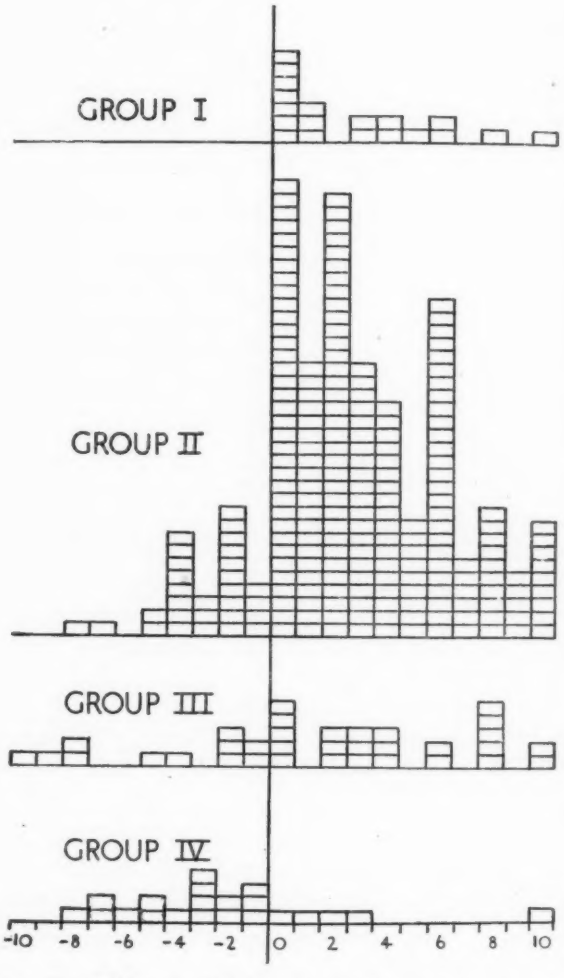

FIG. 2.—(Tube 1) − (Tube 4). Variance ratio 10·67. Each rectangle represents a single individual.

Let A_{11}, A_{12}, etc., be the total sums of squares and cross products, and a_{11}, a_{12}, etc., the sums of squares and cross products between groups; then the coefficients for the readings in tubes 1, 2, and 4 are found from the equations:

$$b_1(A_{11}-\phi a_{11})+b_2(A_{12}-\phi a_{12})+b_4(A_{14}-\phi a_{14})=0$$
$$b_1(A_{21}-\phi a_{21})+b_2(A_{22}-\phi a_{22})+b_4(A_{24}-\phi a_{24})=0$$
$$b_1(A_{41}-\phi a_{41})+b_2(A_{42}-\phi a_{42})+b_4(A_{44}-\phi a_{44})=0$$

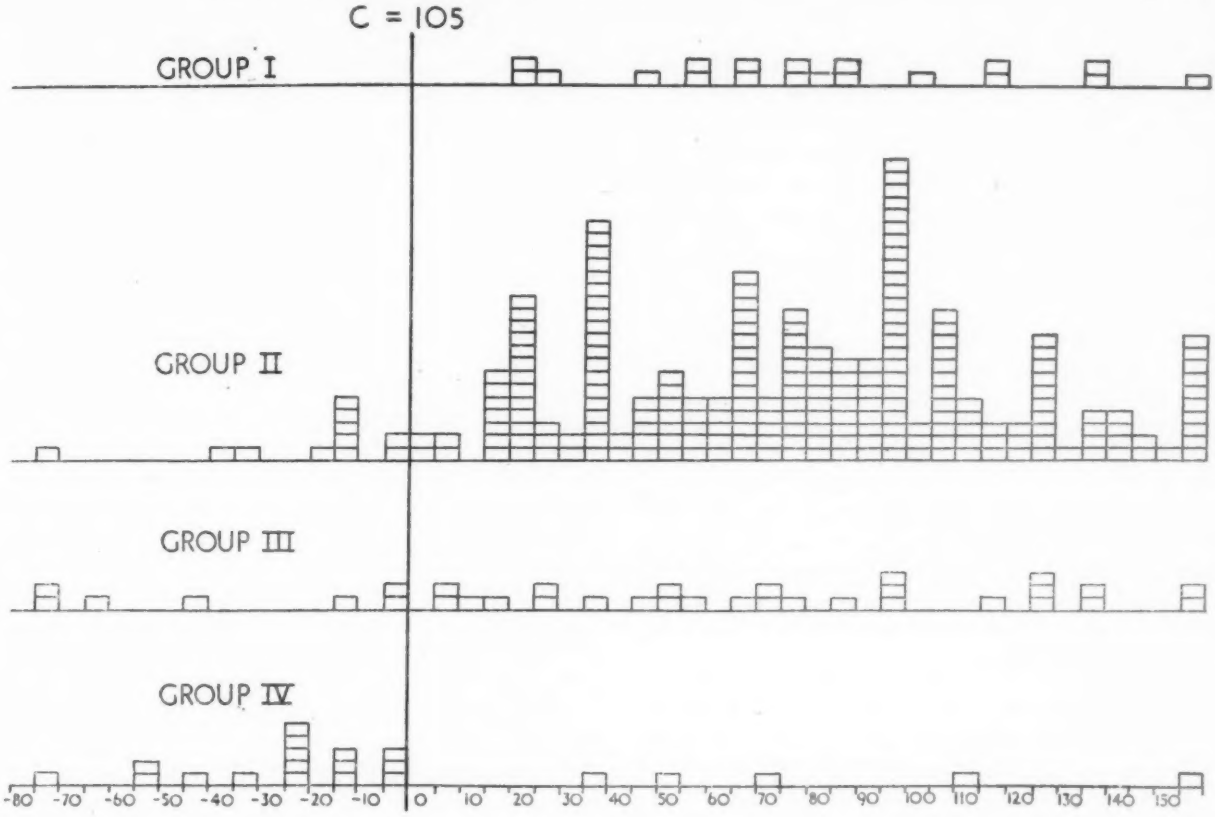

FIG. 3.—Discriminant function. $y = 105 + (\text{Tube } 1) - \frac{1}{2}(\text{Tube } 2) - 1\frac{1}{2}(\text{Tube } 4)$. Variance ratio 16·77. Each rectangle represents a single individual.

ϕ is estimated by evaluating the determinant

$$\begin{vmatrix} A_{11}-\phi a_{11} & A_{12}-\phi a_{12} & A_{14}-\phi a_{14} \\ A_{21}-\phi a_{21} & A_{22}-\phi a_{22} & A_{24}-\phi a_{24} \\ A_{41}-\phi a_{41} & A_{42}-\phi a_{42} & A_{44}-\phi a_{44} \end{vmatrix} = 0$$

For the present material (using the percentage haemolysis readings in units of grouping ranging from 0 to 10) this is:

$$\begin{vmatrix} 4318\cdot45118-\phi 15\cdot43964 & 2391\cdot60606+\phi 1\cdot61057 & 1651\cdot45791+\phi 20\cdot33504 \\ 2391\cdot60606+\phi 1\cdot61057 & 2498\cdot54545-\phi 18\cdot49606 & 1155\cdot21212-\phi 84\cdot22895 \\ 1651\cdot45791+\phi 20\cdot33504 & 1155\cdot21212-\phi 84\cdot22895 & 3757\cdot36027-\phi 414\cdot08803 \end{vmatrix} = 0$$

which yields:

$$155{,}980{,}507 - 23{,}766{,}775\cdot9\phi + 113{,}045\cdot085\phi^2 - 55\cdot1013107\phi^3 = 0$$

The lowest root is the one needed. This is:

$$\phi = 6\cdot7809485$$

Substituting in the above equations:

$$\begin{aligned} 4213\cdot75578b_1 + 2402\cdot52725b_2 + 1789\cdot34877b_4 &= 0 \\ 2402\cdot52725b_1 + 2373\cdot12462b_2 + 584\cdot05995b_4 &= 0 \\ 1789\cdot34877b_1 + 584\cdot05995b_2 + 949\cdot44883b_4 &= 0 \end{aligned}$$

There are actually two equations relating the three coefficients, so only their relative magnitudes can be determined. This, however, is all that is required. Putting $b_1 = 1$, we find:

$$\begin{aligned} b_1 &= 1 \\ b_2 &= -0\cdot64642653 \\ b_4 &= -1\cdot48696473 \end{aligned}$$

Functions of this type do not appear to be sensitive to moderate changes in the magnitudes of the coefficients, hence b_2 and b_4 can be rounded off to $-\frac{1}{2}$ and $-1\frac{1}{2}$ respectively; this reduces the variance ratio by less than 1 per cent. (In the calculations, however, it is necessary to carry a relatively large number of figures.) As is explained below, the best practical use of the function is for distinguishing "probably positive" from "probably negative" sera, instead of attempting any further sub-division. Scrutiny of the figures indicates that a suitable constant is 105; so the discriminant function is:

$y = 105 + (\%$ haemolysis in tube 1$) - \frac{1}{2}(\%$ haemolysis in tube 2$) - 1\frac{1}{2}(\%$ haemolysis in tube 4$)$

A positive answer or zero is taken to indicate a

probably positive result; a negative answer a probably negative result.

Table IV gives the analysis of variance. The mean squares and cross-products of columns three to eight are calculated in the usual way. The mean squares for the discriminant function are calculated by using the coefficients determined above. Thus the mean square between groups is given by:

$$(b_1^2 \times 5 \cdot 147) + (b_2^2 \times 6 \cdot 165) + (b_4^2 \times 138 \cdot 029) + (2b_1b_2 \times -0 \cdot 537) + (2b_1b_4 \times -6 \cdot 778) + (2b_2b_4 \times 28 \cdot 076)$$

This for the squares and products of coefficients taken to five places of decimals gives the figure of 387·739 shown in the column headed X^2 and for the rounded off coefficients the figure of 380·239 shown in the column headed X_1^2. The variance ratio of 16·77 in this column checks, as it must do, with the variance ratio calculated directly from the individual values used in preparing Fig. 3. Similarly, the last column is calculated by putting $b_1 = 1$ and $b_4 = -1$. For the mean square between groups:

$$(1 \times 5 \cdot 147) + (1 \times 138 \cdot 029) + 2(-1 \times -6 \cdot 778) = 156 \cdot 732$$

Again the variance ratio of 10·67 checks with the variance ratio calculated directly from the individual values of Fig. 2.

We have, then, the rather remarkable result that although tubes 1 and 2 are by themselves useless for the further classification of doubtful sera, yet in combination with tube 4 they yield a function having a substantial advantage over that tube used alone. Furthermore, owing to the possibility of rounding off the coefficients with only trivial loss of information, it is a very simple function which can be applied in a moment in the laboratory. Table V shows the result of using the function in this way for the 297 doubtful sera.

TABLE V

DISCRIMINATION OF 297 DOUBTFUL SERA ATTAINED BY USE OF FUNCTION

Group	Probably positive $y \geqslant O$	Probably negative $y < O$	Per cent. probably positive
I	19	0	100
II	212	11	95
III	27	7	79
IV	5	16	24

The three figures illustrate graphically the discrimination between the clinical groups secured by the three methods (1) the reading in tube 4, (2) the simple difference method—tubes 1 and 4, (3) the discriminant function.

It will be noted that statistical analysis confirms theoretical expectation, in that the most important feature of the function turns out to be the difference in the readings in tubes 1 and 4. The function, just like the difference method, makes all previous full negatives with anything less than complete haemolysis in tube 4 probably positive. The principal advantage lies in a resorting of some of the sera doubtful by the standard technique. A previous full positive remains probably positive unless the haemolysis in tube 4 is 80 per cent. or more. This seems a sensible result; the highest haemolysis in the five such sera of the present series was 40 per cent. An advantage of the function which is not perhaps fully reflected by the variance ratios is the greater range of values; as haemolysis is measured in steps of 10 per cent., the readings in tube 4 and the difference method lead to a limited and somewhat inflexible set of figures. This is well illustrated in the figures; group II—the most important group—is well spread out instead of being crowded closely against the boundary line.

The distribution of the percentage haemolysis figures, as shown in the appendix tables, is markedly non-normal; in fact it tends to be J- or U-shaped. Yet, as so often happens, the application of straightforward linear methods has given a useful result. In view of this no attempt has been made to find a more complex function. There is no simple way of doing this; any appreciable improvement is very problematical; and in any event such a function would lead to a formula that would be too complicated for rapid laboratory use. The non-normal distribution of the variables has one consequence, however. It would be unsafe to rely too closely on the actual magnitude of the answer; a large figure, positive or negative, does not necessarily indicate a more positive or more negative result than one somewhat nearer zero. In practice this is no disadvantage. The recommended international reporting, using the standard technique, is to classify sera into three groups only: positive, negative, and doubtful. There could be no question of setting up a considerable number of categories; two intermediate ones are enough. At the Essex County Hospital Pathology Laboratory we now simply report the intermediate sera, according to the figure given by the function, as "doubtful (positive by the modified technique)" or "doubtful (negative by the modified technique)."

APPENDIX TABLES

HAEMOLYSIS READINGS IN THE THREE TUBES FOR THE 297 SERA WITH PARTIAL HAEMOLYSIS IN AT LEAST ONE TUBE
(Units of grouping: 0, 1, 2, ... 10 represent percentage haemolysis 0, 10, 20 .... 100.)

GROUP I

Tube 1 \ Tube 2	0	1	2	3	4	5	6	7	8	9	10	
0		1			2		1				1	5
1												
2					1						1	2
3	1											1
4												
5												
6											2	2
7												
8											1	1
9											2	2
10											6	6
	1	1			3		1				13	19

GROUP I

Tube 1 \ Tube 4	0	1	2	3	4	5	6	7	8	9	10	
0	5											5
1												
2			2									2
3	1											1
4												
5												
6	2											2
7												
8	1											1
9							1		1			2
10	1					1	2			2		6
	10		2			1	3		1	2		19

GROUP I

Tube 4 \ Tube 2	0	1	2	3	4	5	6	7	8	9	10	
0	1	1			2		1				5	10
1												
2					1						1	2
3												
4												
5											1	1
6											3	3
7												
8											1	1
9											2	2
10												
	1	1			3		1				13	19

GROUP II

Tube 1 \ Tube 2	0	1	2	3	4	5	6	7	8	9	10	
0	3	1	8	3	6	2	3	3	3	1	2	35
1		2	3	1		1			1	1		9
2	1		1	1	4		2		1		5	15
3			1				1			1		3
4				1	1	2	1		1	2	5	13
5								2			2	4
6			1				2		1		6	10
7									3	1	6	10
8								1	1	3	26	31
9							1			1	6	8
10				1						1	83	85
	4	3	14	7	11	5	10	6	11	11	141	223

GROUP II

Tube 1 \ Tube 4	0	1	2	3	4	5	6	7	8	9	10	
0	25		3	1	4	1		1				35
1	4	2		1		1	1					9
2	9	1	2	1	1						1	15
3	2						1					3
4	6		4		2				1			13
5			1				1	1		1		4
6	4		1	2		1			1		1	10
7	1	1			5		1			1	1	10
8	4	2	8	3	3	2	3		3	1	2	31
9	2		2	1			1		1		1	8
10	9	3	6	1	12	6	8	8	18	13	1	85
	66	9	27	10	27	11	16	10	24	16	7	223

GROUP II

Tube 4 \ Tube 2	0	1	2	3	4	5	6	7	8	9	10	
0	1	2	11	5	8	4	6	3	3	2	21	66
1			1						1	1	6	9
2	1				3		2		1	2	18	27
3	1	1					1		1		6	10
4	1		1			1	1		1	1	21	27
5				1						1	9	11
6			1						1	1	13	16
7								1	1	1	7	10
8								1		1	22	24
9								1	1	1	13	16
10				1					1		5	7
	4	3	14	7	11	5	10	6	11	11	141	223

GROUP III

Tube 1 \ Tube 2	0	1	2	3	4	5	6	7	8	9	10	
0	2			1		1	1					5
1												
2									2	1	1	4
3												
4							1				1	2
5												
6											4	4
7											1	1
8							1				4	5
9											4	4
10											9	9
	2			1		1	3		2	1	24	34

GROUP III

Tube 1 \ Tube 4	0	1	2	3	4	5	6	7	8	9	10	
0			1		1	1				1	1	5
1												
2	1		1								2	4
3												
4	2											2
5												
6				1	1		2					4
7					1							1
8	2								1		2	5
9						1				1	2	4
10	2		3		2			1	1			9
	7		5	1	5	2	2	1	2	2	7	34

GROUP III

Tube 4 \ Tube 2	0	1	2	3	4	5	6	7	8	9	10	
0							1		1		5	7
1												
2	1									1	3	5
3											1	1
4	1										4	5
5						1					1	2
6											2	2
7											1	1
8											2	2
9				1							1	2
10							2		1		4	7
	2			1		1	3		2	1	24	34

GROUP IV

Tube 1 \ Tube 2	0	1	2	3	4	5	6	7	8	9	10	
0										1		1
1												
2				1		1					1	3
3									1			1
4											2	2
5						1					1	2
6									1			1
7											4	4
8											2	2
9											3	3
10											2	2
				1		2			2	1	15	21

GROUP IV

Tube 1 \ Tube 4	0	1	2	3	4	5	6	7	8	9	10	
0						1						1
1												
2	1									1	1	3
3											1	1
4					1						1	2
5					1						1	2
6											1	1
7											4	4
8											2	2
9											3	3
10	1							1				2
	2				2	1		1		1	14	21

GROUP IV

Tube 2 \ Tube 4	0	1	2	3	4	5	6	7	8	9	10	
0				1							1	2
1												
2												
3												
4						1					1	2
5										1		1
6												
7											1	1
8												
9						1						1
10									2		12	14
				1		2			2	1	15	21

REMAINING 703 SERA

	0 (all tubes)	10 (all tubes)
Group I	44	5
Group II	92	216
Group III	18	88
Group IV	3	237

SUMMARY

An attempt has been made to assess the value of a modification of the standard Wassermann reaction by applying it to 1,000 difficult sera divided into four clinical groups representing decreasing proportions of true sero-positive syphilis. A function which maximizes the variation between groups relative to that within groups was found to give a substantial improvement in discrimination as compared with other methods of using the readings. It is suggested that more use might be made of discriminant function analysis with multiple groups: a technique which must have many applications in a wide variety of biological problems.

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THE STATISTICAL SPECIFICITY OF A CODE PERSONNEL CYPHER SEQUENCE

BY

LANCELOT HOGBEN and KENNETH W. CROSS

Some system of personnel identification suitable for mechanical recording is a necessary prerequisite alike for large-scale statistical research involving recourse to original records of the patient and for administrative requirements with respect to cross reference of successive admissions to the same or to different institutions. The desiderata of a code appropriate to this end have been the subject of a previous communication by the writers,* who have put forward a proposal which entails recourse to a 10-cypher sequence requiring nine columns of the customary punch-card system. The main features of the Birmingham proposal are as follows:

(i) to employ information of a sort which is immediately accessible in the sense that the record officer must in any case obtain it—accordingly, information of a sort which it would otherwise be necessary to record independently;

(ii) to use only such information as is referable to *unchanging* characteristics of the individual, such as birth date and sex;

(iii) to allocate information embodied in the code as far as possible in accordance with the principle of equi-partition in the sense that any one of 10^9 cypher sequences constitutes a class of approximately equal frequency in the population at large.

In this context, it is unnecessary to traverse previous discussion with respect to the implementation of (iii), which presupposes that any specification associated with a particular run of integers constituting a sample of information allocated to a particular block has an approximately equal chance of association with information specified by a particular sequence of integers belonging to an adjacent block of the cypher sequence. If it is in fact possible to do so, we are then able to formulate an exact solution of the problem: how often would it happen that the number of individuals receiving one and the same code number embodying a given number of cyphers would not exceed a given value in a population of a given size?

The End in View

In stating the issue thus, we have to bear in mind that our end in view is twofold:

(*a*) to minimize space allocated on a record card to the identification of the individual to whom it refers with due regard to the exigencies of mechanical aids to sorting, tabulation, and collation;

(*b*) to minimize effort entailed in extracting from original documents in a central file information not included in the duplicate punch card for routine returns or for *ad hoc* enquiries.

Evidently, no code can ensure that two or more individuals never receive one and the same label. All we can ask from a code is that: (*a*) it will greatly reduce the labour of identifying in a central file several thousand individuals who have the same patronymic; (*b*) it will make such identification possible without excessive demands on punch-card column space requisite for specification of more essential information. Relevant data on the original records, for example full name and address or for purposes of mechanical collation *date of admission*, will always safeguard the possibility of confusing two individuals who receive the same label.

The Code in Operation

At the operational level our problem is in part a time-and-motion study. It is a matter of seconds to scrutinize five cards with the same code number in a file arranged numerically with a view to ascertaining whether they refer to different persons. It is not a matter of seconds to extract from a file of all living persons in England, alphabetically arranged in accordance with their surnames, a particular Smith among about 200,000 Smiths of the same sex,

* "Identification of Medical Documents", *Brit. med. J.*, April, 1948, vol. 1, p. 632.

many of them with the same first name. We shall therefore accomplish a considerable economy of office routine, if we can ensure odds of over 1,000 to 1 against the occurrence of as many as five individuals with one and the same code number.

In formal terms, the conditions of the problem raised above are as follows:

(*a*) for a population of k individuals l different labels are available;

(*b*) every one of the k individuals receives one label at random;

(*c*) there is no restriction on the use of one and the same label repetitively.

What we now want to know is how often it will happen that *no more than p* individuals receive one and the same label. In conformity with (*c*), the allocation referred to in (*b*) signifies the existence of an assemblage of k labels classifiable as follows:

x_1 are *unique*
x_2 occur *twice*
x_3 occur *three* times
x_p occur p times.

Accordingly, the number of *different* labels attached to the k items will usually be less than k. We shall call it d; and may then write:

$$d = x_1 + x_2 + x_3 \ldots . x_p = \sum_{1}^{p} x_r \qquad \text{(i)}$$

$$k = x_1 + 2x_2 + 3x_3 \ldots . p.x_p = \sum_{1}^{p} r.x_r \qquad \text{(ii)}$$

The multinomial which defines the frequency distribution of the allocation of l labels to k individuals with no restriction on the number who may receive one and the same label is:

$$l^{-k}\,(1+1+1+1 \ldots . l \text{ terms})^k \qquad \text{(iii)}$$

To get the required frequency, that is, that of the class which has no label allocated to more than p individuals, we shall denote by x_p the number of labels each repeated p times in a k-fold set, the maximal realizable value of x_p being $m_p = (k \div p)$ Likewise the maximal realizable value of x_{p-1}, the number of labels each repeated $(p-1)$ times is $m_{p-1} = (k - p.x_p) \div (p-1)$ and so on. We may define a k-fold set as *unique* if it fulfils both of two conditions: (*a*) that $x_1, x_2 \ldots . x_p$ each has a unique numerical value; (*b*) that the denomination of the particular labels of each of the sub-sets respectively composed of $x_1, x_2 \ldots . x_p$ labels is itself unique.

The term in (iii) definitive of a unique set so defined is:

$$k! \div l^k \prod_{r=1}^{r=p} (r!)^{x_r} \qquad \text{(iv)}$$

Now the number of terms which fulfil *only* the first condition (*a*) stated above, that is, that the numerical values of $x_1, x_2, x_3 \ldots . x_p$ are unique, is itself the number of ways of choosing x_p out of l different labels for repetition p times, x_{p-1} out of the residual $(l - x_p)$ for repetition $(p-1)$ times and so forth. If we denote by d the number of different labels in the k-fold set in accordance with (i) the number of ways of choosing the class which is unique only in accordance with (*a*) above is:

$$\binom{l}{x_p} . \binom{l - x_p}{x_{p-1}} . \binom{l - x_p - x_{p-1}}{x_{p-2}} \ldots . \binom{l - d + x_1}{x_1}$$

$$= l! \div (l-d)! \prod_{r=1}^{r=p} (x_r!) \qquad \text{(v)}$$

From (iv) and (v) we obtain the frequency $P(x_p)$ of all k-fold sets consistent with the condition that we allocate x_p labels p times, x_{p-1} labels $(p-1)$ times and so on:

$$P(x_p) = k!\, l! \div l^k (l-d)! \prod_{r=1}^{r=p} (r!)^{x_r} (x_r!) \qquad \text{(vi)}$$

This is the sum of all terms definitive of: (*a*) the allocation of no label more than p times; (*b*) the allocation of x_p labels exactly p times, x_{p-1} labels exactly $(p-1)$ times and so on. What we finally want to find is the probability that the k-fold set of labels will contain no particular label more than p times, that is, the frequency $(P_{p \cdot k \cdot l})$ of getting a sample in which x_p can have any value from 0 to m_p as defined above, x_{p-1} can have any value from 0 to m_{p-1} and so forth. This is the sum of all terms in which no label occurs more than p times with no restriction on x_p, x_{p-1}, etc., between the limits 0 and m_p, m_{p-1}, etc., that is to say:

$$P_{p \cdot k \cdot l} = k!\, l! \div l^k \sum_{x_p=0}^{m_p} \cdot \sum_{x_{p-1}=0}^{m_{p-1}} \cdot \sum_{x_{p-2}=0}^{m_{p-2}} \ldots .$$

$$(l-d)! \prod_{r=1}^{r=p} (r!)^{x_r} (x_r!) \qquad \text{(vii)}$$

In this expression as above:

$$d = \sum_{r=1}^{r=p} x_r$$

$$m_{p-r} = \left[k - \sum_{s=0}^{s=r-1} (p-s) x_{p-s} \right] \div (p-r)$$

The summation of (vii) is laborious, and we have to thank Dr. J. C. P. Miller of the *Scientific Computing Service* for investigating its numerical properties of

which a few examples will suffice for our purpose. For reasons which follow it will be enough to cite $P_{p\cdot1,000\cdot5,000}$, that is, the probability of repetition of some of 5,000 labels allocated to 1,000 individuals at least p times but none more than p times.

Any code which employs a run of cyphers specifying the birth date of the individual ensures that no two individuals will have the same code number unless born on the same day. A ten-cypher code which assigns 6 cyphers to the birth date and allocates the remaining 10,000 labels in equal numbers to males and females respectively in accordance with the principle of equipartition indicated above, thus provides a selection of 5,000 labels with which to specify individuals of the same sex born on the same day. In England alone, daily birth of individuals of the same sex is at present little more than 1,000. Accordingly, the problem of the specificity of the Birmingham code is that of defining the frequency with which no one of $l=5,000$ labels distributed at random among $k=1,000$ individuals will occur more than p times. By recourse to (vii) we obtain the following numerical results for different values of p:

$$P_{2\cdot1,000\cdot5,000}=0\cdot00281$$
$$P_{3\cdot1,000\cdot5,000}=0\cdot75331$$
$$P_{4\cdot1,000\cdot5,000}=0\cdot98887$$
$$P_{5\cdot1,000\cdot5,000}=0\cdot99963$$

We may set out these results more explicitly:

No cypher sequence will be allocated to more than:	*Approximate odds against the occurrence:*
3 individuals	3 : 1
4 *ditto*	100 : 1
5 *ditto*	2,000 : 1

If we assume that every individual at some time in the course of his life enters a medical institution, we thus arrive at the following conclusion: in a national file based on the Birmingham code the odds are about 100 : 1 that as many as four individuals and about 2,000 : 1 that as many as five individuals with the same cypher designation would ever occupy the same niche, and their separate identities would of course be immediately distinguishable by other particulars recorded.

With due regard to earlier remarks concerning what we can reasonably hope to achieve by using a numerical code of the sort under discussion, the result stated in the last paragraph signalizes no mean advantage. However, it grossly understates the possibility of ensuring the separate identification of individuals by using as much essential information as we have at our disposal. If the date of admission (five-cypher sequence) *immediately follows* a personal code number prescribed in the publication cited earlier, it is possible to use the first fourteen columns of the card in a sort for collation of individual cases or for the preparation of a *nominal* role for back-reference to a central file (*vide* Truelove and Hogben, *this journal*, vol. 1, p. 18). Of these fourteen columns, only the two referable to the patronymic at birth in fact embody information of an exclusively personal kind. The other twelve specify particulars, including sex and age, essential to the completion of *any* medical document.

Dr. Enid Charles, Head of the Statistical Office of the Birmingham Corporation, has raised some minor issues which the earlier publication did not in fact deal with. By her permission we take this opportunity of citing a personal communication, the contents of which we fully endorse.

ADDENDUM

BY

ENID CHARLES

1. *Babies with no Christian names:*

A baby, particularly an illegitimate one, is often a hospital case and therefore requires a code number from the moment of birth. The Christian name does not become official until the birth is registered, which of itself creates a difficulty.

I have made a study of 1,500 illegitimate births registered in Birmingham in the twelve-month period 1945-1946. In many of these the birth registration was considerably delayed, up to as much as eleven months after birth. Over 1% of the births registered during the period were not registered until over three months after birth. A more serious difficulty is that in eleven registrations no Christian name at all was given, and three of those died very soon after birth so presumably never had a name. I suggest that this difficulty could be met by coding the males with unknown Christian names XX and females with unknown Christian names YY. A further difficulty is in the case of twins of the same sex, both dying within a few hours of birth and having no Christian names. These would receive the same code number and it is quite possible that the medical records could be exactly the same; the only distinguishing feature I can think of would be the *exact* time of birth.

2. *Adoptions:*

In 1946-1947 there were 24,000-25,000 births annually in Birmingham. In 1946 there were 603 Adoption Orders, and in 1947, 484. This involves a legal change of surname, and I presume

in this case the only thing to do will be to recopy all previous medical records relating to this baby with a new code number.

There is another type of case which might be considered, though it occurs in very small numbers. Among the illegitimate births previously referred to there *appear* to have been nine cases in which the baby was registered in the mother's name but the parents later married. Most, if not all, of these babies could have been legitimated. In any case whether legally legitimated or not it would be undesirable to retain the original surname. But whereas Adoption Orders are a matter of record, this last category would be troublesome to track down. All these points have arisen in my own work, seeing that we keep track of all illegitimate babies continuously up to at least 5 years old and so will have to come to a decision on these points if we use the medical code number.

3. *Change of name by Deed Poll or on Naturalization:*

Though these cases are infrequent, a decision will have to be reached on them.

4. *Entries in Code C:*

Proposed entries IA—IZ, VA—VZ, etc., would appear easier to refer to if entered simply as I, V, etc.

5. *Misprints in code as printed in the British Medical Journal:*

(*a*) *Code A.*

Delete *Dais* with number.

(*b*) *Code B.*

For I (excluding above) . . . 76 *read* I (excluding above) and J (excluding below) . . . 76.

For W (excluding Winifred) . . . 96 *read* W—Z (excluding Winifred) . . . 96.

REVIEWS

Maternity in Great Britain. A Survey of Social and Economic Aspects of Pregnancy and Childbirth undertaken by a Joint Committee of the Royal College of Obstetricians and Gynaecologists and the Population Investigation Committee. 1948. Geoffrey Cumberlege, Oxford University Press. Pp. 252+xvi with 47 tables and 7 diagrams. Price 12*s.* 6*d.*

This book presents the results of an enquiry into various aspects of pregnancy and childbirth carried out with the co-operation of the medical officers of health of 424 local authorities in Great Britain. The material presented in the book is based mainly on interviews conducted by health visitors with nearly 14,000 women who bore children in a specified week in 1946. In addition to this questionnaire survey, more intensive studies were carried out in five selected areas: Aberdeen, Croydon, Kent, Lewisham, and Wolverhampton.

The purpose of this enquiry was to provide information concerning the following matters: (*a*) availability of the maternity services to different social classes and in different parts of the country; (*b*) the use made of these services; (*c*) their effectiveness in educating mothers and in reducing mortality and morbidity amongst mothers and infants; (*d*) the need for domestic help during pregnancy and the puerperium; (*e*) the nature and extent of present-day expenditure on childbirth.

The following are the chief findings.

Municipal antenatal services are used by all sections of the community. Thirty-one per cent. of women supervised by their own private doctors and one-third of the expectant mothers in the most prosperous group make use of them. Seventy-three per cent. are supervised under local authority schemes; 54 per cent. at clinics; 5 per cent. by general practitioners working for local authorities; and 14 per cent. by municipal midwives. The most satisfactory antenatal supervision would seem to be given at clinics. In rural areas as a whole there is evidence of inadequate provision of facilities for local authority antenatal care.

Far too many expectant mothers do not place themselves under the supervision sufficiently early in pregnancy. Many do not do so until the last three months. Routine attendance should begin in the first trimester of pregnancy. At the present time less than half the expectant mothers attend as early as this. Once an expectant mother has come under supervision she will in the majority of cases attend regularly. Women in full-time work during pregnancy do not receive less antenatal care than non-working mothers. Many leave their work soon after becoming pregnant. It would seem to be shown by the evidence collected that regular antenatal supervision when begun sufficiently early in pregnancy can effectively reduce the incidence of prematurity and neonatal death and increase the likelihood of establishing breast-feeding.

In different parts of the country there is great variation in the proportion of women entering hospital for their confinement. Difficulties are created by the scarcity of hospital beds and of home helps and residential nurseries. The result is that many confinements take place in appalling conditions of overcrowding. There is, however, no evidence that overcrowding itself increases the actual risks of delivery. Home delivery carries a low risk of stillbirth and neonatal death, but these rates are very high amongst those who, having been originally booked for home delivery, are admitted as unbooked cases to hospital. An opinion survey amongst the most prosperous group of mothers, comparatively free to choose where they shall be confined, suggests that hospital beds should be made available for at least 70 per cent. of births. This demand for hospital accommodation is created by the provision of such accommodation, for many women would prefer a good domiciliary midwifery service provided housing conditions were improved and domestic help made available. On the other hand, if institutional maternity beds were provided and if provision were made for the care of older children during the lying-in period there is little doubt that the institutional habit would become as established in Britain as it has become in America. The alternatives, therefore, would seem to be an increase in institutional maternity beds on the one hand, and on the other general improvements in housing and the establishment of an efficient home help service.

Relatively few general practitioners undertake domiciliary midwifery except amongst the more prosperous groups. Even under the Scottish maternity scheme less than a quarter of home deliveries are actually carried out by doctors. The average Scottish mother is discharged from hospital on the tenth day, the average English mother on the thirteenth.

The main complaint by mothers in this enquiry was directed against the lack of analgesia in childbearing. In the Metropolitan boroughs only 5 per cent. of mothers confined at home and 48 per cent. of those confined in hospital are given this relief. In home confinements in Great Britain as a whole only 8 per cent. of the women attended by midwives are given analgesia as compared with 48 per cent. of those attended by doctors. Relief of pain is thus most frequently available to those who can afford a medical practitioner to deliver them. Combining all social economic groups, analgesia is given only to some 20 per cent. of those delivered at home. The low incidence of analgesia in cases attended by midwives is due to difficulties in transport and to a shortage of suitably trained persons. Only slightly more than half of those delivered in hospital are given relief. Staff shortage is usually the excuse offered.

Childbearing is a cause of much avoidable ill-health. Postnatal examination made four to six weeks after every birth would undoubtedly lower this morbidity. Far too few women, however, avail themselves of the existing facilities for such examination. This is particularly so for those who are confined at home in the charge of a midwife.

Fifty-seven per cent. of the babies covered by this survey had been taken to infant welfare centres before they were two months old. All social classes make frequent use of this service, and even in the most prosperous group attendance reached the level of 48 per cent. Household duties are the most important obstacles to the use of these centres, and the provision at centres of playrooms for older children would encourage more mothers to attend. In rural areas transport difficulties prevent many from bringing their babies. These have in certain areas been overcome through the provision of special transport.

Pregnancy and childbirth involved all socio-economic groups in very heavy expenditure, especially in the case

of the first child. For the well-to-do the average cost was £57, for the manual worker £36. Poorer mothers economized progressively as their families grew in size. A high proportion of the total expenditure in all groups went to purchase non-medical items such as layette and pram. Statutory grants and allowances covered only a very small proportion of the total expenditure. Even when the new rates become available, the grant will still cover only a small proportion of the total costs. The first stage toward the removal of the economic obstacles to childbearing is the provision of free confinement care. But total costs can be substantially reduced only if mothers are assisted also with their non-medical expenditure. Reference is made to the Swedish system whereby low-income families can apply to a special fund for additional aid for specified items, including clothing, equipment, dental care, additional food, and domestic help up to a maximum of around £27.

Of all single births in the sample, 6·4 per cent. were premature. The causes of such prematurity were partly biological and partly economic. Prematurity was less frequent amongst mothers aged 25 to 35. Birth intervals of less than two years predisposed to premature birth. Women who had worked outside the home during the last five months of pregnancy more frequently had premature babies than those who had not so worked or had left work during the first four months.

By the end of the eighth week 43 per cent. of mothers were bottle-feeding their babies. Contrary to general belief, babies were more often successfully breast-fed when they had been born in hospital. The main failure was in establishing lactation. The establishment and maintenance of lactation depends more on the quality of antenatal supervision than on care given during the puerperium. Such antenatal supervision is more important than any other factor, biological, social, or economic, that was considered.

The great majority of married women in full-time gainful occupations during pregnancy were primigravidae. They usually terminated their employment in mid-pregnancy and only a small proportion of them had resumed work on a date two months after delivery. The few remaining at work during the later stages of pregnancy were exposed to rather greater risks of stillbirth and prematurity than were women not in employment, although they used antenatal services to the same extent. Expectant mothers compelled by economic necessity to continue earning in late pregnancy did not receive enough assistance from current maternity grants to enable them to leave work without financial loss.

Domestic help is essential to give mothers a chance of resting during the later weeks of pregnancy and after confinement, but many women were not receiving such assistance. Even the well-to-do were not always receiving help, but lack of help was much more frequent in the poorer groups, especially amongst multiparae confined at home. Seventy per cent. of the mothers intended to seek the services of a municipal home help at their next confinement if such were available.

Unmarried mothers first came under antenatal supervision at a later stage of pregnancy and some received no antenatal care at all. They were rarely delivered by doctors, and therefore were even less likely to receive any form of analgesia than were the manual workers' wives. Economically the unmarried mother is at a great disadvantage. Leaving work commonly results in destitution. Most of them had to return to full-time work soon after the birth of their child. Many decided to bring up their babies in their own homes.

The report concludes with the presentation of a number of recommendations the nature of which is clearly indicated by the findings recorded above. It reveals many hidden defects of the existing organization, and the recommendations made for improvement are essentially practical. It is intimated that since this enquiry was limited to the study of pregnancy and labour and the first two months of the puerperium, and in order to make a complete assessment of the achievements of the maternity services, a follow-up survey of maternal morbidity and of the social and economic factors affecting infant health and development during the first two years of life is to be undertaken.

There can be no doubt of the value of this report, which includes a great amount of information which is made available for the first time. It can claim to be of special interest to the medical profession and to all others who are concerned with the employment of medicine as an instrument of social policy.

F. A. E. CREW

Textbook of the Rheumatic Diseases. Edited by W. S. C. COPEMAN, O.B.E., M.D., F.R.C.P. 1948. Edinburgh: E. and S. Livingstone. Pp. 619 with 351 illustrations. Price 50*s.* net.

Social Medicine interests itself particularly in the relationship of the social environment to disease. There are diseases in the aetiology and dissemination of which the social environment is implicated and there are others which, because of their nature and incidence, result in problems which affect society as a whole and which for their solution demand adequate social action. The inclusion of a chapter on the statistics of rheumatic diseases in this most comprehensive textbook shows that these demand the interest of social medicine no less than that of clinical.

It is recorded that out of 16·7 million days of incapacity for work within a year amongst insured men, muscular rheumatism accounted for 220,000 days, lumbago for 194,000, rheumatoid arthritis for 131,000, osteo-arthritis for 64,000, subacute and articular rheumatism for 40,000, rheumatic fever for 11,000, chorea for 4,000, together with arthritis (unspecified) 201,000 and rheumatism (unqualified) 702,000. These are the figures given in the report on *Incapacitating Sickness in the Insured Population* issued by the Department of Health for Scotland in 1937-8. Dr. Percy Stocks, who is responsible for this chapter, calls attention to the need for accuracy in diagnosis and for a standardization of simple classification if statistical investigation is to be profitable.

The figures of Hedley (1940) on rheumatic heart disease in Philadelphia hospitals are quoted to show that in 39 per cent. of people with a history of rheumatic fever the onset of rheumatism occurred before the age of 10, and in 63 per cent. before the age of 15. In 39 per cent. of people with a history of rheumatic heart disease the onset of that condition occurred before the age of 10, and in 58 per cent. before the age of 15.

The records maintained by the Emergency Medical Services during 1942-4 show that the contributions to total illness amongst men made by osteo-arthritis and muscular rheumatism increased rapidly as age advanced, whilst those of rheumatic fever declined. Amongst men under 25, two-fifths of all rheumatic illness consisted of rheumatic fever and its sequelae, one-fifth being other forms of arthritis, and two-fifths muscular or undefined. At ages 35-44 rheumatic fever contributed less than

one-tenth, other arthritis about a quarter, and muscular types over three-fifths.

The statistics of sickness in the Civil Service of Canada in 1937-8 and 1938-9 show that rheumatic fever accounted for about 4 out of 1,000 of all illnesses causing certificated absence from work, and chronic arthritic rheumatism and other arthritis for about 19 per 1,000.

The records of the Emergency Medical Services 1942-3 show that half the men were still in hospital under treatment or convalescent after a lapse of nearly three months from the date of first admission to hospital in the case of rheumatic fever, that for other arthritic rheumatism the median duration was eight or nine weeks for young men and about six weeks for older men, and for muscular rheumatism it was three weeks for young and four weeks for older men.

A hospital discharge study of all patients leaving New York hospitals in the year 1933 revealed that out of 576,623 who had been treated as in-patients there were 2,097 with a diagnosis of rheumatic fever without heart affection, 3,852 with rheumatic heart disease (of whom 1,835 had rheumatic fever), 610 with Sydenham's chorea, and 6,209 with arthritic conditions.

The Canadian Civil Service statistics for years just before the war showed that the average duration of certificated absence from work was about twenty-four days for rheumatic fever and twenty-two days for chronic arthritic rheumatism.

Rheumatic fever is a notifiable disease in Denmark. The annual notification rate during 1938-43 averaged 74 per 100,000 persons. A comparable rate for England and Wales would be 30,000 cases annually, about 7 out of every 1,000 infants born would have rheumatic fever before the age of 15, and subsequently another 38 attacks would be expected amongst the survivors.

The records of the London County Council for 1938 suggest that about 2·5 per cent. of London's child population were suffering from or had experienced some form of rheumatic infection.

Estimates derived from samples of men between 18 and 41 rejected by Medical Boards from military service suggest that about 7 per cent. of rejections were on account of heart disease of rheumatic origin and that 6 or 7 per 1,000 of all men of those ages had been sufficiently incapacitated by rheumatic fever to cause rejection.

The social survey on behalf of the Ministry of Health during 1944-5 revealed that the reported incidence of rheumatism was higher amongst women than men, the female excess amounting to about 40 per cent., more than this under 25 and less from 35 to 44. With advancing age from 20 to 60 the rate increased eight-fold in men and seven-fold in women. The disability rate per 1,000 men was about 5 per 1,000. An excess in frequency was shown in the group with ample house room. Thirteen per cent. recorded rheumatism out of 1,767 people with only one or two people in the household compared with 10 per cent. out of the 4,062 with three, four, or five in the household and 9 per cent. out of the 891 with six or more in the household. These differences were not to be explained by any suggestion that the smaller households consisted largely of older people. The work of Daniel is quoted. He found that there was a clearly defined inverse relation between incidence and number of persons per room, families with less than 0·6 of a room per person having 3 to 4 times the rate of families with 1·4 or more rooms per person. A similar correlation was found with the net income reckoned as a percentage of the minimum needs of the family. There would appear to be no important difference between urban and rural incidence for total rheumatism.

The mortality caused by rheumatic conditions arises mainly by heart lesions left by it. Dr. Stocks again discusses the effect of variety in death certification upon profitable statistical investigation. The crude death rate of women from rheumatic fever declined steadily during the early part of the war. Amongst men, despite the fact that the civilian rates were prejudiced by selection, there was a decline from 1938 to 1942 followed by a rise in 1943 and 1944. The rates are maximal at ages 10 to 14 and higher amongst females between 5 and 10. After 35 neither age nor sex makes any marked difference to the rate.

There could be nothing more indicative of the value of the co-operation of the medical statistician and the clinician than the place that this particular chapter claims in this book, nine-tenths of which is concerned with attempts to cope with the clinical problems caused by the rheumatic diseases. In this chapter the clinician will find ample means for the checking of his own hypothecation concerning aetiology, whilst the investigator, medical or social, will find abundant invitations to profitable research.

F. A. E. CREW

Disorders of Sex and Reproduction. By A. P. PILLAY, O.B.E., M.B., B.S. 1948. London: H. K. Lewis. Pp. 299+xiv with 5 photographs and 2 graphs. Price 18*s*.

Since sexual disharmonies are the cause of so much distress in a modern society and are so heavily responsible for the insufficiencies of certain social institutions, this book has its value to such as are concerned with the social aspects of disease, and though it does not deal either with the incidence of the various disorders of sex in the population or with the effects of such diseases on social affairs, nevertheless, despite its purely clinical approach, it can claim to be of interest to the social scientist.

F. A. E. CREW

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109 KINGSWAY, LONDON, W.C.2; AND ASHFORD, KENT

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